A Dissertation on

NEUTROPHIL TO LYMPHOCYTE RATIO AS A MARKER OF ACUTE EXACERBATION AND DISEASE SEVERITY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Dissertation Submitted to

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032

With partial fulfillment of the regulations

for the award of the degree of

M.D. GENERAL MEDICINE

BRANCH-I

COIMBATORE MEDICAL COLLEGE,

COIMBATORE

MAY 2018

DECLARATION

I Solemnly declare that the dissertation titled "**Neutrophil to lymphocyte ratio as a marker of acute exacerbation and disease severity in chronic obstructive pulmonary disease"** was done by me from JULY 2016 to JUNE 2017 under the guidance and supervision of **PROF. Dr S.USHA M.D.**

This dissertation is submitted to **The Tamilnadu Dr.M.G.R. Medical University** towards the partial fulfilment of the requirement for the award of MD degree in General Medicine (Branch 1)

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CERTIFICATE

Certified that this is the bonafide dissertation done by **Dr. ANOOP PAULOSE** and submitted in partial fulfillment of the requirements for the Degree of **M.D.,General Medicine**, Branch I of **The Tamilnadu Dr. M.G.R. Medical University, Chennai.**

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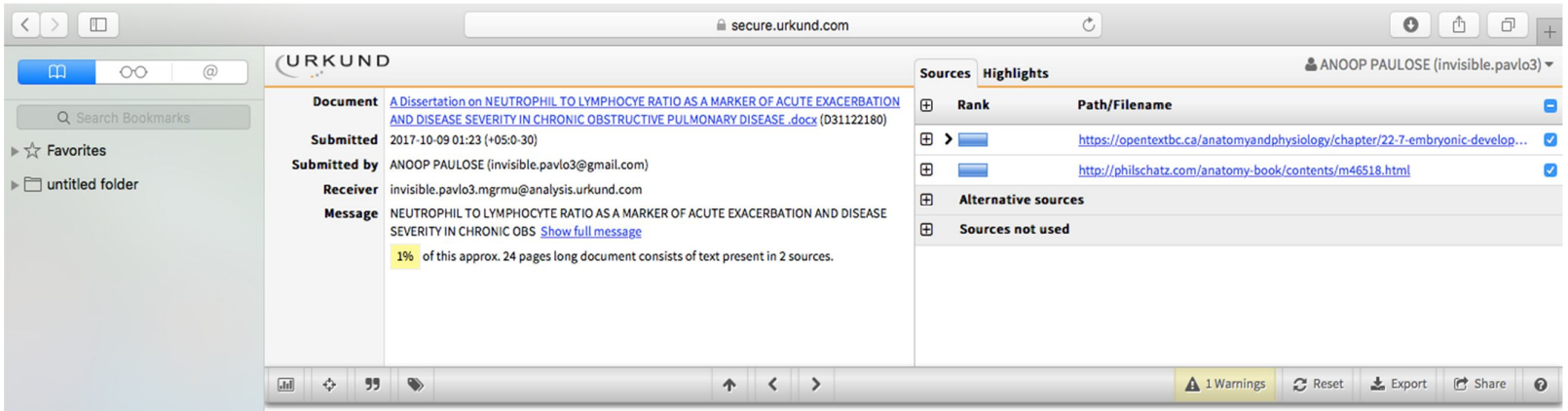

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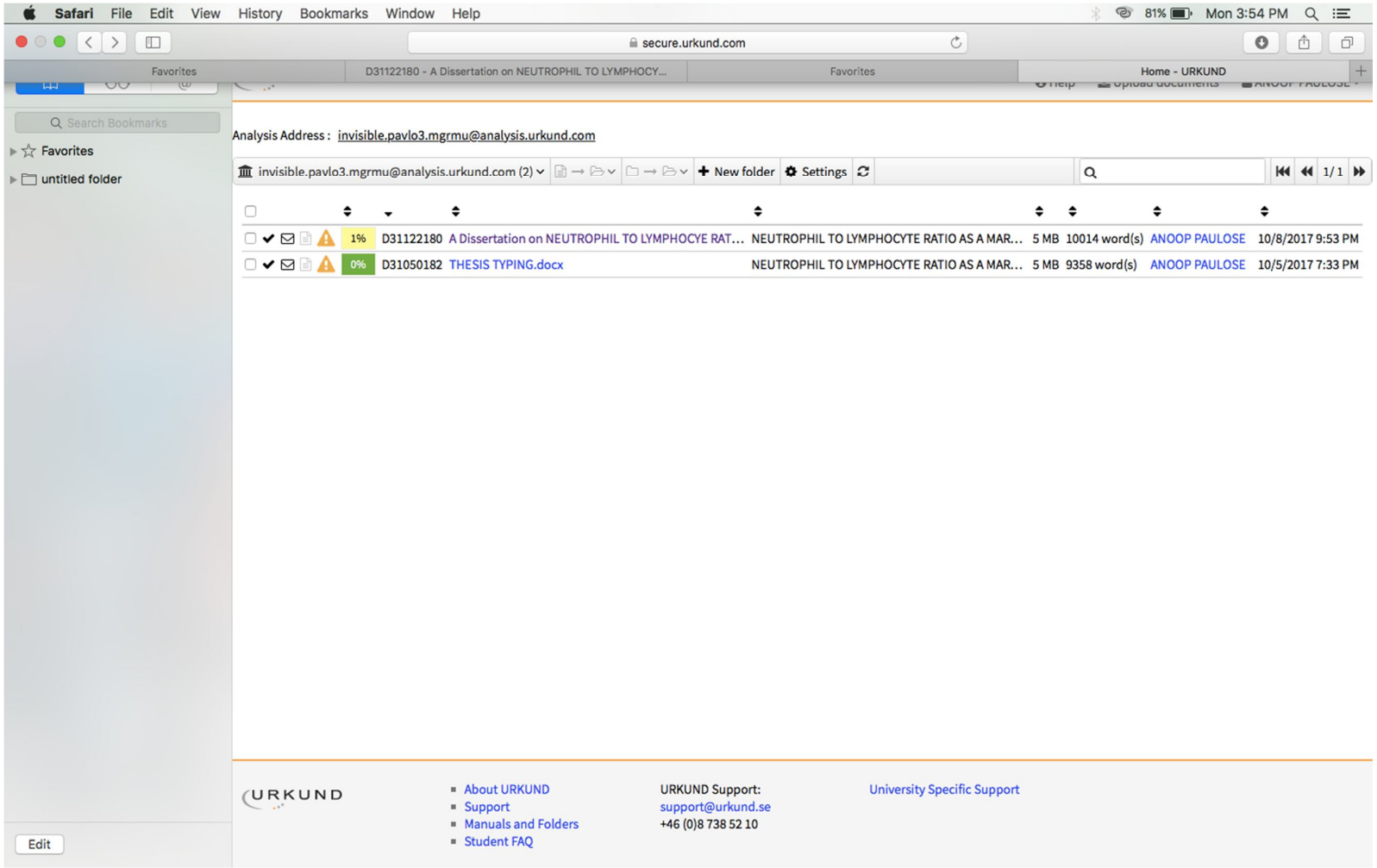
INTRODUCTION

Chronic obstructive pulmonary disease is regarded as the most important public health problem that affect our part of the world. It is the fourth leading cause of mortality in the world, and by 2020 will become the next cause next to ischemic heart disease and stroke as per WHO. COPD mostly affecting males, who are mainly smokers and characterized by limitation of airflow which is not fully transformable to normal, along with increased long term inflammatory response in airways of the tracts of lungs, being viral and bacterial pathogens as the prime cause of exacerbations. Macrophage and cells lining the mucous membrane activation which produce proteinases and chemokines which attract other inflammatory and immune cells, interleukin 8 (IL8), and TNF alpha are released in turn cause attraction of neutrophils to the site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Lastly, I am ever grateful to the **ALMIGHTY GOD** for always showering His blessings on me and my family

Dr. ANOOP PAULOSE

LIST OF ABBREVIATIONS USED

- COPD - Chronic Obstructive Pulmonary Disease
- NLR - Neutrophil Lymphocyte Ratio-
- HRCT - High resolution computed tomography
- BODE - Body Mass Index, Airflow Obstruction, Dyspnea and Exercise
- FEV1 - Forced Expiratory Volume in One second
- FVC - Forced Vital Capacity
- WHO - World Health Organisation
- GOLD - Global Initiative for Chronic Obstructive Lung Disease
- MMRC - Modified Medical Research Council
- BMI - Body Mass Index
- 6WMT - Six Minute Walk Distance
- PAH - Pulmonary Artery Hypertnsion

TABLE OF CONTENTS

LIST OF TABLES

LIST OF CHARTS

LIST OF FIGURES

INTRODUCTION

Chronic obstructive pulmonary disease is regarded as the most important public health problem that affect our part of the world. It is the fourth leading cause of mortality in the world, and by 2020 will become the next cause next to ischemic heart disease and stroke as per WHO. COPD mostly affecting males, who are mainly smokers and characterized by limitation of airflow which is not fully transformable to normal, along with increased long term inflammatory response in airways of the tracts of lungs, being viral and bacterial pathogens as the prime cause of exacerbations. Macrophage and cells lining the mucous membrane activation which produce proteinases and chemokines which attract other inflammatory and immune cells, interleukin 8 (IL8), and TNF alpha are released in turn cause attraction of neutrophils to the site are the main reasons of inflammation that is occurring in COPD.

Neutrophil to lymphocyte ratio (NLR) is a effortless and basic parameter that is readily obtained from the simplest and easy obtainable complete blood count, even in peripheral hospitals. Inflammation is

regarded as a set of interactions between and among immune related cells such as lymphocytes, neutrophils which in turn lead to killing of tissues and destruction which is going on in COPD. One of the inflammatory markers in COPD is NLR and also has its relationship between many disease like, cardiovascular disease, kidney disease, etc.

In this study the association that occurs between acute exacerbation of COPD and NLR is found out which help to asses the morbidity and mortality of condition with out the help of costly investigation, as NLR is easy obtainable investigation and low cost one.

OBJECTIVES OF THE STUDY

- To identify the possible correlation between neutrophil to lymphocyte ratio and severity of COPD.
- To identify correlation between NLR with pulmonary function test(FEV1) in COPD patients.
- To study the prospects of NLR considered to be newer cheaper indicator in acute episodes of COPD.

REVIEW OF LITERATURE

HISTORY – COPD

- COPD was first described by the famous Swiss physician Theophile Bonet back in 1600, In autopsied patients he described about emphysema.

- British born Charles Badham was the first one to use the word “bronchitis” for inflammatory changes of epithelium.

Fig-1-Theophile Bonet

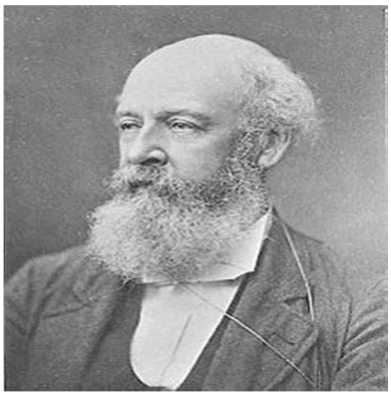


Fig-2 – Charles Badham

- Rene Laennec explained the correlation between chronic bronchitis with emphysema in mid 1800. He described emphysema as damage of the tissues in the air passages.

Fig-3- Rene Laennec with stethoscope

- John Hutchinson is the pioneer in invention of spirometer in 1846.

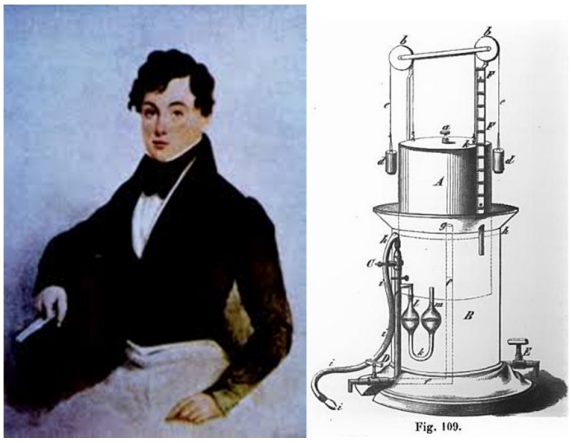


Fig-4- Hutchinson and his Water Spirometer

Hutchinson's instrument was crude one using water which only measured the vital capacity. 100 years' form Hutchinson's spirometer, Tiffeneau added the timed vital capacity to lung function test which measures the airflow.

- In 1959, at a symposium of doctors named a Ciba Guest meeting of doctors and health professional's they made definition of component's which constitute COPD.
- The term FEV1 was first considered to find out expiratory flow in 1960.
- Gaensler who was inspired by Tiffeneau's work added forced vital capacity, become the core of spirometry-FEV1 and FEV1/FVC we use presently.
- Dr. William Briscoe -now considered as the one who used the word COPD in 1965.
- Osler's textbook of medicine in early 1900 describes about emphysema.

EMBRYOLOGICAL FORMATION OF RESPIRATORY SYSTEM

Following fertilization of ova and sperm, the GROWTH of human body can be staged into two divisions

1. **embryonic period-**includes the first 8weeks, where all major organs start to develop
2. **fetal period-**rest of the intrauterine life from 32 weeks where the developed organs mature.

Germinal layers

- **ENDODERM**
- **MESODERM**
- **ECTODERM**

From these three germinal layers all tissues in the body are developed.

Visceral pleura which is covering the external surface of lung develops from the mesoderm while, parietal pleura which is in proximity with the body cavity develops from somatic mesoderm. The cavity is the area in between parietal and visceral pleura.

Weeks 4–7

The origin of the lungs starts at week 4 of intrauterine life. Ectodermal tissue which is present at the front part of head region gradually invaginate posteriorly forming the olfactory pits, these olfactory pits then join further with developing pharynx endodermal tissue. An **olfactory pit** which is seen anteriorly grow further to form the nasal cavity. Concurrently the formation lung bud happens The **lung bud** resembles like a dome-shaped structure which is composed of tissue

that protrudes from the foregut. The **foregut** is formed from endoderm lying just inferior part of the pharyngeal pouches. The **laryngotracheal bud** is an extension which originates from the lung bud. The part of laryngotracheal bud which is in proximity with the pharynx transforms to the trachea, while those which lie at terminal part transforms into bulbous, transforming into bronchial buds. A **bronchial bud** then forms all other lower respiratory tissues and the bronchi.

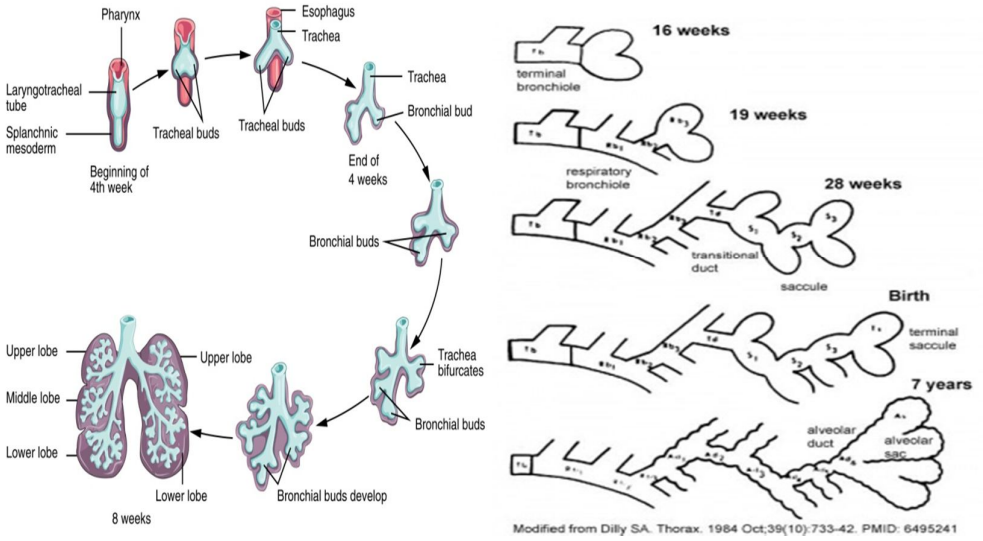


Fig No-5-Formation of the Lower part of Respiratory System.

Weeks 7–16

Branching of bronchial buds is ongoing until all of the segmental bronchi development completes. At about 13th week, the lumens inside the bronchi stats to grow further in size. By week 16 of gestation period,

respiratory bronchioles are developed. All the major structures of the lung are formed by this stage.

Weeks 16–24

After the respiratory bronchioles development occurs, extensive vascularization, as along with the emergence of alveolar ducts and precursors of alveolar cells happens. Then cells which cover respiratory structures starts to transform into two types of cells type I along with type II pneumocytes. After the complete development of type II cells, they begin their function of secretion of the substance called pulmonary surfactant which is the reason and prime factor for lowering surface tension in lugs. At about 20th week of gestation breathing movements of fetus begins to occur.

From Weeks 24 till term of pregnancy

More and more amount of precursor cells of alveoli develop, more pulmonary surfactant production happens. Blood vessels of pulmonary system have formed and continue to expand, which results in big surface area which will aids to gas exchange. While the development going through seventh month, adequate numbers of capillaries are produced which aid in gas exchange, and so that a of an infant born prematurely at this stage will be able to thrive. However respiratory system, development continue to happen till early childhood, when all the things of a mature alveoli occurs.

ANATOMY

Respiratory system consists of

1. upper respiratory tract
2. lower respiratory tract

UPPER RESPIRATORY PATHWAY

Components include the following- nasal cavity, pharynx, para nasal sinus and larynx.

Functions of upper airway tract are

1. Act as a conduct for air flow
2. Filtering, heating, conditioning of air, protection of airways, phonation, coughing olfaction and taste, also muscle action helps in swallowing.

LOWER RESPIRATORY PATHWAY

Trachea

Trachea also called as windpipe which is about 5 inch tube formed by C shaped rings consisting of hyaline cartilage starts from cricoid cartilage and then divides into two at level corresponding to angle of louis in superior mediastinum and is covered by pseudo stratified ciliated columnar type of epithelium. It has 16 – 20 cartilaginous rings, which

protect the air passage from collapsing. Trachea bifurcates at carina to form the left side main bronchus which is about5cm long and right side bronchus 1– 2.8 cm long. The right bronchus is more in diameter, with small length and almost placed vertically compared to the left. So right lung is the most common site of aspiration rig. Both the two bronchi then pass to the lungs before branching into smaller sized secondary and then to tertiary bronchi. Further secondary bronchi splits into tertiary which again divide into millions of minute terminal bronchioles.

The zone which conducts air of respiratory tract is up-to 16th division, followed by respiratory zone up-to 23rd division of respiratory tract.

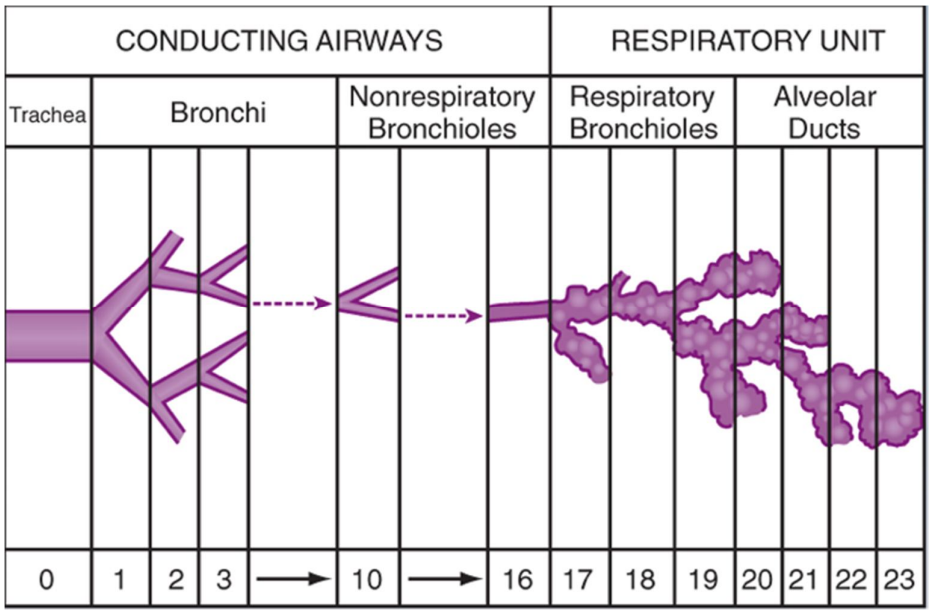
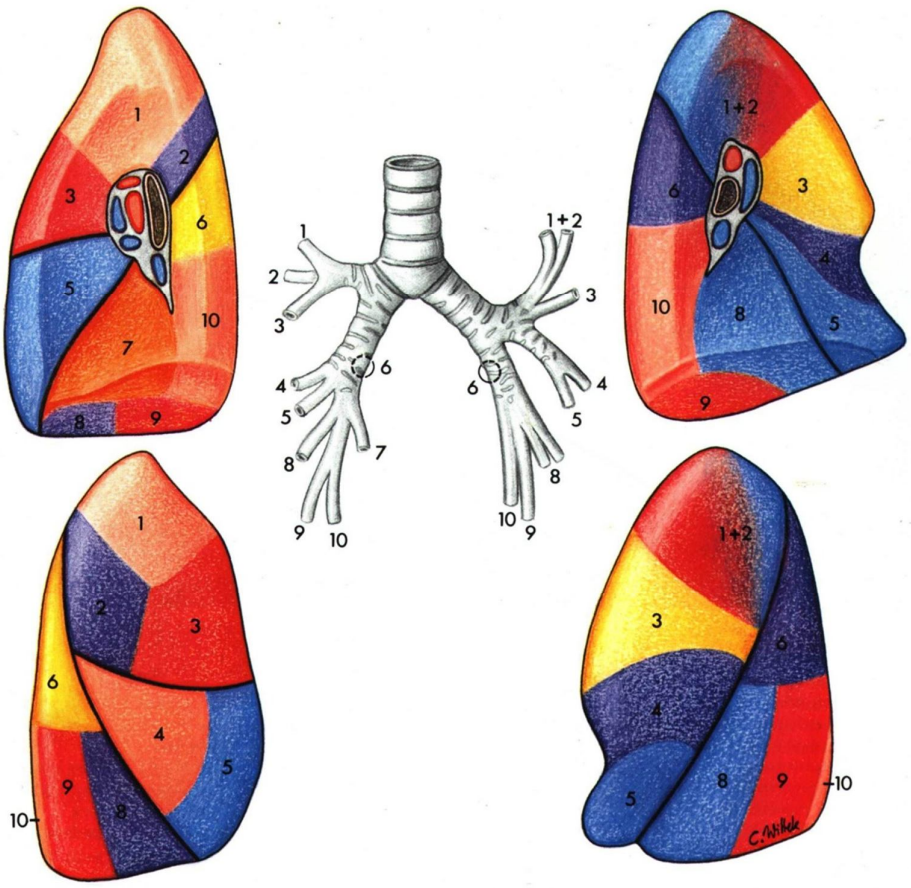


Fig No:6- Conducting and Respiratory units of lung

BRONCHOPULOMONARY SEGMENTS



Distribution of bronchopulmonary segments of the lungs and their relation to the bronchial tree (after J. F. Huber).
The bronchopulmonary segments are morphologically and functionally separate independent respiratory units of the lung tissue. Each segment is surrounded by connective tissue which is continuous with the visceral pleura. The segmental bronchi in a segment are central, closely accompanied by branches of the pulmonary arteries whereas the tributaries of the pulmonary veins run **between** the segments. Thus, the veins serve two adjacent segments which drain for the most part into more than one vein. A bronchopulmonary segment is therefore not a complete vascular unit, but segmentation is the result of a specific architecture of the lung vasculature.

Right lung		**Left lung**	
1 Apical segment 2 Posterior segment 3 Anterior segment	Upper lobe bronchus	1+2 Apico-posterior segment 3 Anterior segment	Superior division → Upper lobe bronchus
4 Lateral segment 5 Medial segment	Middle lobe bronchus	4 Superior lingular segment 5 Inferior lingular segment	Inferior division → Upper lobe bronchus
6 Superior (apical) segment 7 Medial basal segment 8 Anterior basal segment 9 Lateral basal segment 10 Posterior basal segment	Lower lobe bronchus	6 Superior (apical) segment 7 Absent 8 Anteromedial basal segment 9 Lateral basal segment 10 Posterior basal segment	Lower lobe bronchus

Fig No:7- Broncho pulmonary Segments

ALVEOLI

The terminal respiratory unit.

Six hundred million alveoli are occurring in the lungs. Its epithelium consists of 2 types of cells.

 Type 1 cells – lining cells- these are flat cells, which are squamous epithelial cells and form over 95% of surface of alveoli.

 Type II cells- Pneumocytes whose main function is to secrete surfactant; whose main function is to reduce surface tension inside the alveoli

also these cells act as reserve cells which can transform to type I pneumocytes when required.

PULMONARY CIRCULATION

Venous blood coming from the right atrium enters into right ventricle through the atrio-ventricular valves and then moves through the pulmonary artery's to reach pulmonary capillary bed where oxygen moves into the RBC occurs. The oxygenated blood, moves through pulmonary veins in turn reaching into the left atrium, from left atrium

passes to the left ventricle and to aorta and major arteries of the body thereby oxygenating the body.

The lungs therefore have dual blood supply-

1. Bronchial arteries which give oxygenated blood
2. Venous blood from pulmonary arteries.

In lungs some mixing of blood occurs, so that if one side of circulation gets blocked, blood supply to pulmonary parenchyma is supplied by the other vessel. Bronchial arteries then divide to capillaries, and then they empty into bronchial vein and then to azygos vein.

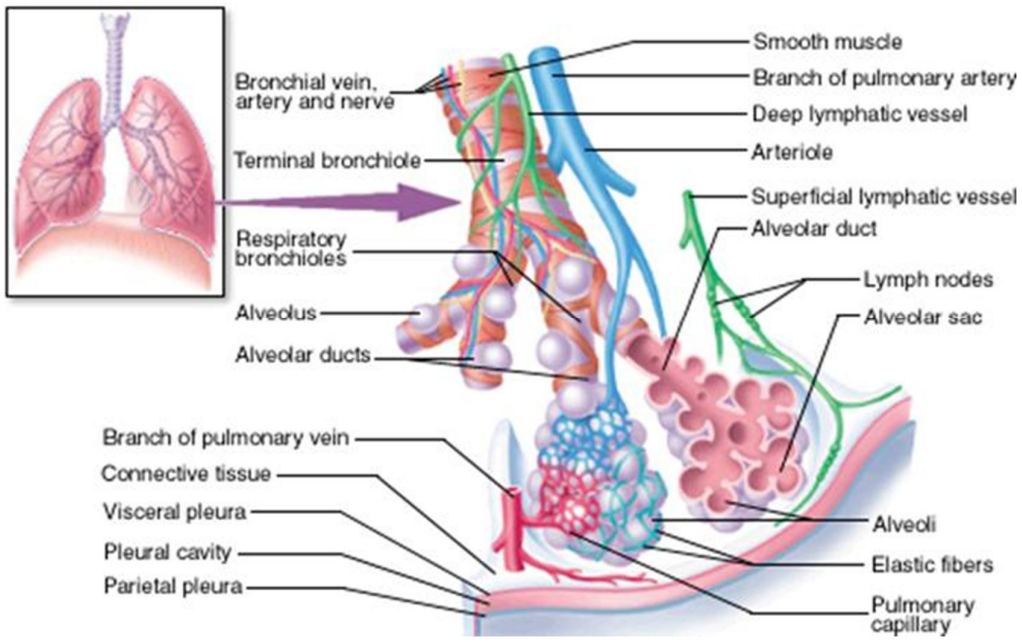


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Fig No: 8-Pulmonary Circulation

LYMPHATIC SYSTEM

Lymphatic's in the respiratory system grossly divided in to

1. SUPERFICIAL PLEXUS

2. DEEP PLEXUS

- Superficial plexus mainly drain from the viscera covering pleura, while deep plexus from peri -bronchial tissues.
- Alveoli lack lymphatic drainage.
- Lymphatic's flow towards hilum and further to the extra pulmonary lymph nodes, which empty's lymph into the thoracic duct.

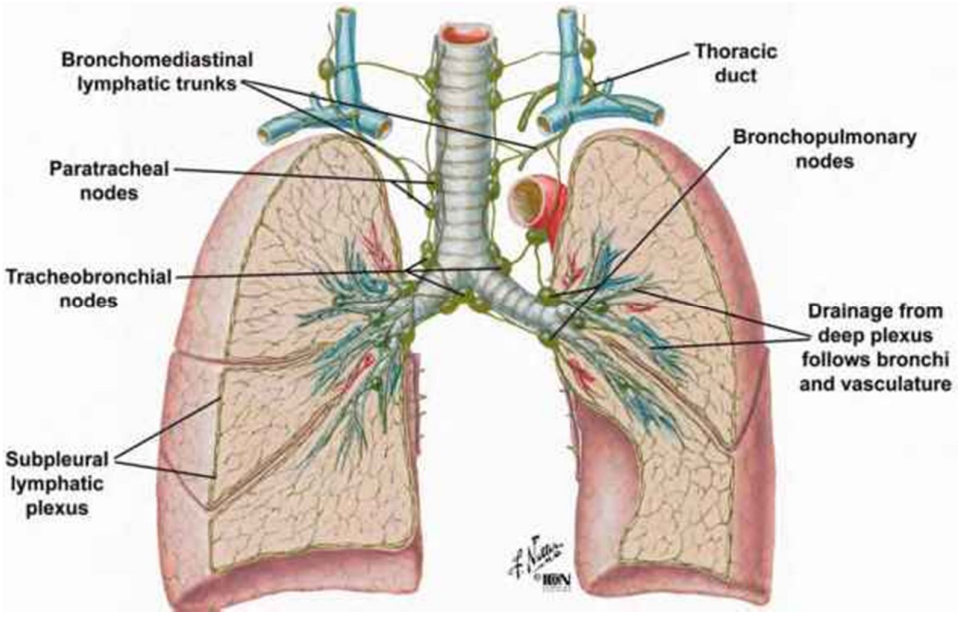


Fig No: 9- Lymphatic drainage of Lungs

PHYSIOLOGY

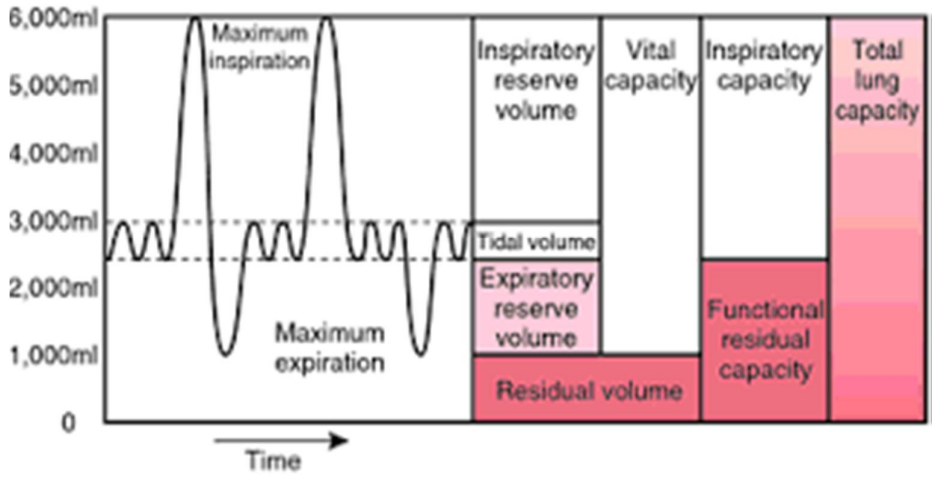


Fig no: 10 - Volumes of Lung and Capacities-Normal Spirogram

Lung volumes

1) Tidal volume: The quantity of air inhaled in or out at a normal resting respiratory cycle (500-750 ml).

2) Inspiratory reserve volume: This is the quantity of air which can be taken in by a persons maximal effort of inspiration, at the end of a normal inspiration (2 liters).

3) Expiratory reserve volume: The quantity of air which can be expelled by a maximum expiratory effort after a person had expired normally normal (1 liter).

4) Residual volume: The quantity of air which is left in lungs after the end of a maximal expiration (value -1.3litres).

Lung Capacities

5) Vital capacity: Quantity of air expelled by maximum expiration after a deep inspiration, called index of lung function (3.5 liters).

6) Inspiratory capacity: It is the maximum air inspired after the end-expiratory level (IRV+ TV) (2.5 liters).

7) Functional residual capacity: The volume of air which remains in the lungs at the end point of normal expiration (RV+ ERV). (Value -2.5 liters).

8) Total lung capacity: It consists sum total of Tidal volume, plus Residual volume plus Inspiratory reserve volume, plus expiratory reserve volume (Value - about 5litres).

Spirogram is the modality which helps in measuring the following things

1. FEV1 (Forced expiratory volume in one second): the quantity of air which an individual can expire in the very first second of maximum expiration after maximum inspiration. It measures how quickly the lungs can exhale air.

2. FVC (Forced vital capacity): maximum quantity of gas an individual can breathe out forcefully.

3. FEV1/FVC: It is a ratio. FEV1 expressed as how much part of the FVC.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

DEFINITION

Chronic obstructive pulmonary disease (COPD): A preventable and treatable disease which consists of constant expiratory limitation of the flow of air which is not fully reversible. A progressive disease, which comprises of enhanced and chronic inflammatory response to gases and noxious materials of the mucosa of respiratory tract.

Detection of COPD is thought in a patient coming with symptoms of cough, excessive production of sputum, or dysponea, and or exposure to factors which causing the disease will be present.

GOLD defines COPD – "Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation

that is due to airway and/or alveolar abnormalities usually caused by significant exposure to gases or noxious particles".

COPD consists of two different types of clinical entities

1. **CHRONIC BRONCHITIS**
2. **EMPHYSEMA.**

They can also occur together.

- Bronchitis is defined as occurrence of cough along with expectoration on most days for at least three months in at least two consecutive years and no identifiable cause detected.
- Bronchitis means the **airways** are inflamed and narrowed
- Emphysema as the word indicates defined as abnormal permanent dilatation of alveoli occurring distal to the terminal bronchioles which is associated with wall destruction and without much fibrosis.
- So Emphysema affects the **air sacs**.

Thus, chronic bronchitis definition is on the basis of clinical features, while emphysema is defined on morphological basis.

As airways are narrowed, the movement of air become harder as it moves in and moves out during breathing, and so lungs are not that much able to acquire oxygen and exchange carbon dioxide from the lungs. In a healthy lung, the tissue which lies in between stretches back so as to keep airways open during normal respiration. In COPD patients**,** the airways get narrowed because of the following reasons:

- Less retraction force on the airways as the lung tissues are damaged.
- Lining of the airways which are naturally elastic wont function.
- Lining of airway is inflamed

CHRONIC BRONCHITIS

Types:

1) Simple chronic bronchitis- is a entity with sputum production mainly mucoid in nature
2) Chronic muco-purulent bronchitis- repeated and constant purulent sputum production who does not have a local supportive disease

3) Chronic asthmatic bronchitis/ chronic bronchitis associated with obstruction- severe dysponea and wheezing associated with inhaled irritants or infections in the setting of bronchitis.

EMPHYSEMA

Emphysema is a disease which occurs when cigarette smoke or other air pollutants, including dust fumes etc, destruct the inter alveolar walls. When the alveoli weaken, their walls get ruptures, creating single air sacs instead of multiple ones which decrease the exchange of oxygen with carbon dioxide.

CLASSIFICATION

A. TRUE EMPHYSEMA

1) Centriacinar- Destruction which occurs in the proximal or central part of respiratory unit(acinus) resulting in its enlargement. Upper lobe and apices predominantly involved. Common in male who smokes.

2) Panacinar- There is consistent destruction along with dilatation of acinus. Lower part of basal zones predominantly involved. Associated with alpha 1-antitrypsin deficiency.

3) Paraseptal- Only the distal acinus is involved. It is seen near pleura which often leads to spontaneous pneumothorax.

4) Irregular(para-cicatrical)- Any type of involvement can occur.

5) Mixed(unclassified) type emphysema

B. OVER INFLATION.

Histologically, the alveoli are dilated and distended or overinflated but septal walls are preserved.

1) Compensatory over inflation (compensatory emphysema)

Compensatory emphysema is a condition in which one part of the lung will increase in size and function, when another part of the lung may be destroyed or functionless. It is seen in clinical conditions such as pneumonias, destroyed lung, large pleural effusions and in pneumothorax. Here, histologic examination shows dilatation and distention of alveolar sac but septal walls are preserved. So in them the term compensatory over inflation is accurate over compensatory emphysema.

2) Senile hyperinflation (Aging lung, senile emphysema)

In old age, the lungs become voluminous because of loss of elastic tissue, thinning and atrophy of ducts of the alveoli along with atrophy of alveoli occurs.

3) Obstructive over inflation (Infantile lobar emphysema)

It is yet another variant of obstructive over inflation occurring in infants in the initial days when a neonate is born who develop respiratory distress or who have congenital hypoplasia of bronchial cartilage. Partial obstruction of respiratory tract mainly in part of bronchial tree (tumor or foreign body) causes over distention of the region supplied by obstructed bronchus. So air enters the while inspiration into the lungs but cannot leave on expiration resulting in ballooning up of the affected areas.

4) Unilateral translucent lung (Unilateral emphysema)

One lung or one of the lobes or segments become radiolucent. The condition occurs in adults. Usually we can elicit a history of serious pulmonary infection in childhood.

5) Interstitial emphysema (Surgical emphysema)

Mediastinal emphysema occurs due to rapid outward release of air into mediastinum following rupture of alveoli. The escaped air leaks into the subcutaneous tissues causing surgical emphysema

Cigarette smoking is considered as one of the important reason which results in COPD according to WHO, the smoke originating from the cigarette consists of many different free radicals along with other oxidant substances, these will cause inflammation in the lining epitheliums of airway tracts and also in the parenchyma of the lung tissue, along with surplus production of mucous decreases the air flow to lungs resulting in COPDs pathological and clinical features. Smoking will reduce the flow rates and decreases the pulmonary function.

Smoking cessation is the most important and the effective treatment of COPD, it decreases the rapidity of development of pulmonary deterioration.

CAUSES OF COPD

Environmental factors

- Tobacco smoke accounts for 95% of cases of development of COPD.

- Indoor air pollution; cooking by using the biomass fuels in confined areas happens in developing countries especially in females of our part of world.
- Occupational exposures, such as coal dust, silica, Cadmium, ammonia
- Reduced birth weight may reduce lung function
- Lung growth: Smoking by mother and infections during childhood period affect growth of lung, leading to decreased lung function
- Infections: recurrent infection may cause decline in FEV1; occurrence of adenovirus in mucosa and lung tissue can cause alteration in local inflammatory response; HIV infection may sometimes associated with the occurrence of emphysema
- Low socioeconomic status
- Cannabis smoking

Host factors

- Genetic factors: α1-antiproteinase deficiency, COPD susceptibility genes
- Airway hyper-reactivity

Risk factors for the development of COPD

- **EXPOSURE TO TOBACCO SMOKE.** Significant and the most important risk factor in the development of COPD is long-term use of cigarette.

- Other variety of tobacco exposure includes – Pipe smokers, chewing tobacco, cigars, electronic cigarettes, marijuana smokers etc.

- **PEOPLE WITH ASTHMA WHO SMOKE.** In them the severity of disease will be even more because of the combined effect.

- **OCCUPATIONAL EXPOSURE TOCHEMICALS AND DUSTS.** The irritation of lung along with progression to COPD can happen in people who are exposed to long term chemical fumes, volatile substance, dusts and vapors.

- **BIO-MASS FUEL AND ITS EFFECTS ON LUNGS.** In mainly developing part of the world, those who inhale the fumes of burning of bio mass fuels for purposes like cooking are more susceptible to develop COPD, and mainly occurs in females as they are more exposed to the same.

- **AGE.** COPD develops gradually and progress. So most of the people in which COPD occurs are above the age group of 40 years.

GENETICS- ALPHA-1 ANTITRYPSIN DEFICIENCY

Normally in people there will be adequate amount of alpha 1 antitrypsin and in some COPD patients accounting about 1 percent, low level of the enzyme is noted because of genetic alterations. Alpha-1-antitrypsin (AAt) is an enzyme which inhibits the serine protease inhibitor and thus by inhibiting neutrophil elastase. The neutrophil elastase is made in the liver and released to blood for its action in the lungs, thus the enzyme deficiency affects two major organs both the liver and the lungs. Individuals with deficient alpha 1 antitrypsin cause emphysema in there third to fourth decades of life.

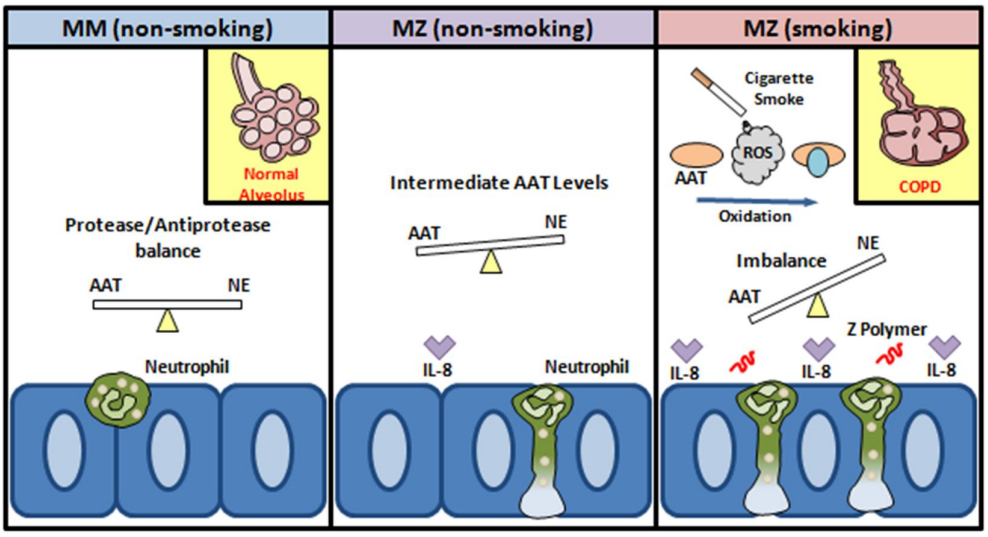


Fig No: 11- Genetics of alpha 1 antitrypsin deficiency

Protease-ant protease hypothesis. Alpha-1-antitrypsin (α1-AT), also called α 1-protease inhibitor (α -1-Pi), is a glycoprotein that forms the

normal constituent in the α 1-globulin part of the plasma proteins on serum electrophoresis. The single gene locus that codes for α -1-AT is whose locus is on chromosome 15th long arm. The normal function of α 1-AT is to inhibit proteases and hence its name α 1-protease inhibitor. The proteases (mainly elastases) are derived from neutrophils. Neutrophil elastase normally in lung tissue is prevented from eating the lung parenchyma because of the anti-elastase activity of the enzyme. So any alterations in the system can results in the pathology occurring in emphysema-By decreased anti-elastase activity i.e. deficiency of α -1 antitrypsin. -By increased activity of elastase i.e. increased neutrophilic activation and also lung infiltration producing more neutrophil elastase.

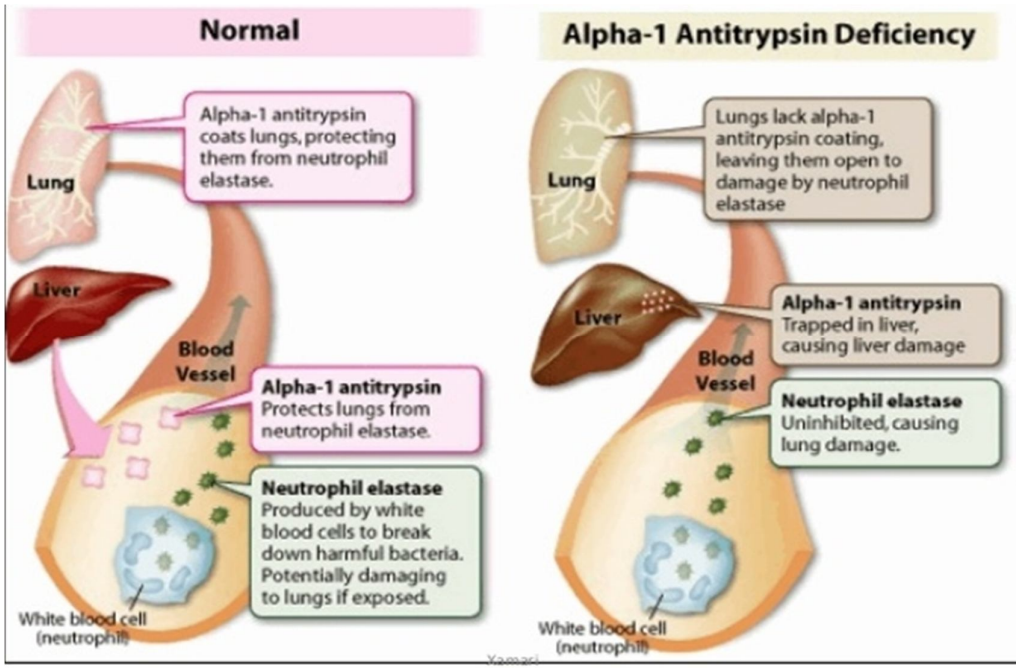


Fig No: 12- Pathogenesis of alpha 1 antitrypsin deficiency

Spirometry – severity of COPD classified on basis of post-bronchodilator FEV1

Gold Stage	Severity	Symptoms	Spirometry
0	At Risk	Chronic cough, sputum production	Normal
I	Mild	With or without chronic cough or sputum production	FEV_1/FVC <0.7 and FEV_1 80% predicted
IIA	Moderate	With or without chronic cough or sputum production	FEV_1/FVC <0.7 and 50% FEV_1 <80% predicted
III	Severe	With or without chronic cough or sputum production	FEV_1/FVC <0.7 and 30% FEV_1 <50% predicted
IV	Very Severe	With or without chronic cough or sputum production	FEV_1/FVC <0.7 and FEV_1 <30% predicted *or* FEV_1 <50% predicted with respiratory failure or signs of right heart failure

Fig No: 13- GOLD staging of COPD

*Lung function should not be the only mandatory thing in diagnosing a patient with mild COPD.

PATHOGENESIS

COPD in most of the patients have simultaneous pulmonary emphysema and chronic bronchitis. Chronic bronchitis does not always lead to emphysema nor all cases of emphysema have the morphological alterations of chronic bronchitis. The relationship that happens in two conditions is principally linked to the common etiologic factors- most

importantly tobacco smoke and air pollutants. Occupational exposure, infection and familial and genetic influences are other less significant contributory factors. However, the main pathology that result in emphysema, is the walls of alveoli get destructed, and is not linked to bronchial changes but is closely related to deficiency of serum alpha-1-antitrypsin, termed protease-anti protease hypothesis.

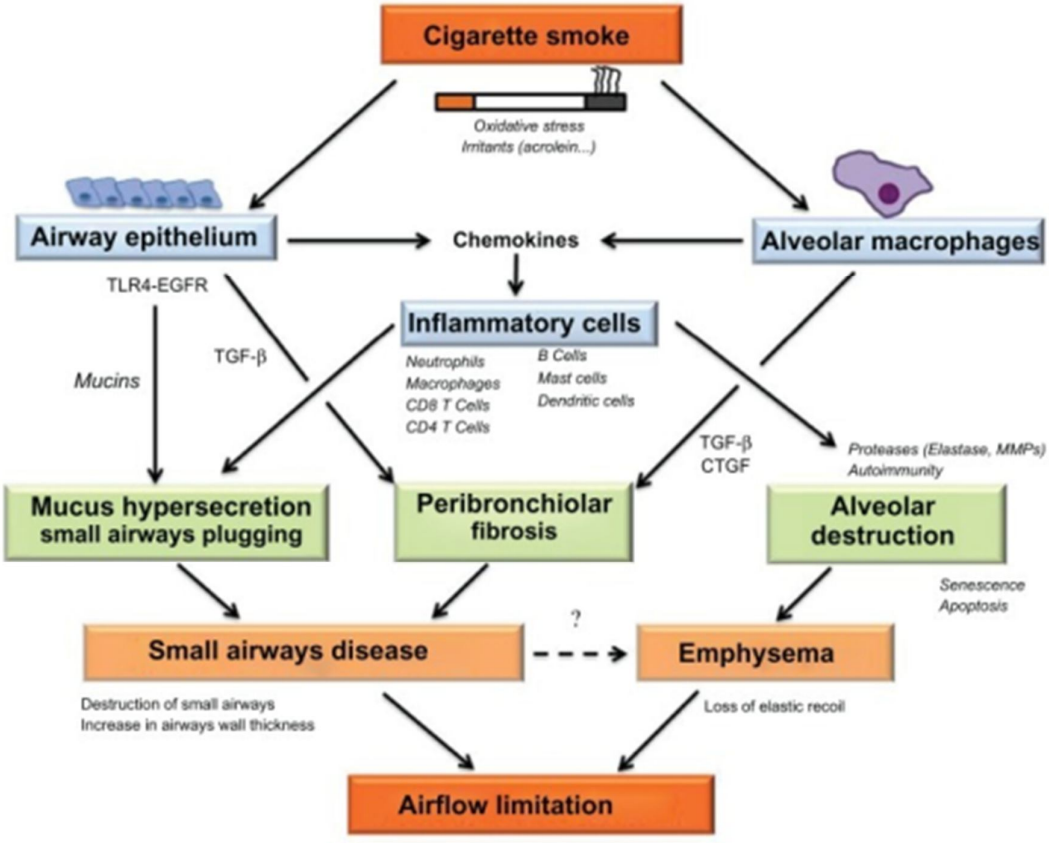


Fig No: 14- Inflammatory pathways in COPD pathogenesis

Factors contributing in COPD pathogenesis are:

1) Inflammation

Chronic inflammation is the specific feature occurring in COPD which is characterized by inflammation in the airways, parenchyma of the lungs, and vascular structures of the lung. Increased neutrophils, Macrophages, CD8+ T-lymphocytes occur in the lung. The inflammatory mediators- leukotriene B4 (LTB4), interleukin 8 (IL-8), tumor necrosis factor alpha are released by the activated cells which can damage lung structures.

2) Proteinases and anti proteinases imbalance causes destruction in walls of alveoli causing emphysema. In alpha 1 anti trypsin low patients (a major protease inhibitor), emphysema develops at a younger age especially in smokers.

Smoking will result in emphysema as a result of increased elastolytic protease in the lungs. These are as under:

- Oxidant in cigarette smoke will cause inhibition of α -1-antitrypsin, as a result of that anti-elastase activity decreases.

- Smokers lungs are rich with neutrophils and phagocytes than the non smoker population; thus they have very high elastase activity.

3) Oxidative stress : Impaction of smoke particles in bronchioles causes inflammatory cell aggregation, increased elastase and decreased alpha 1 antitrypsin resulting in centriacinar emphysema in smokers.

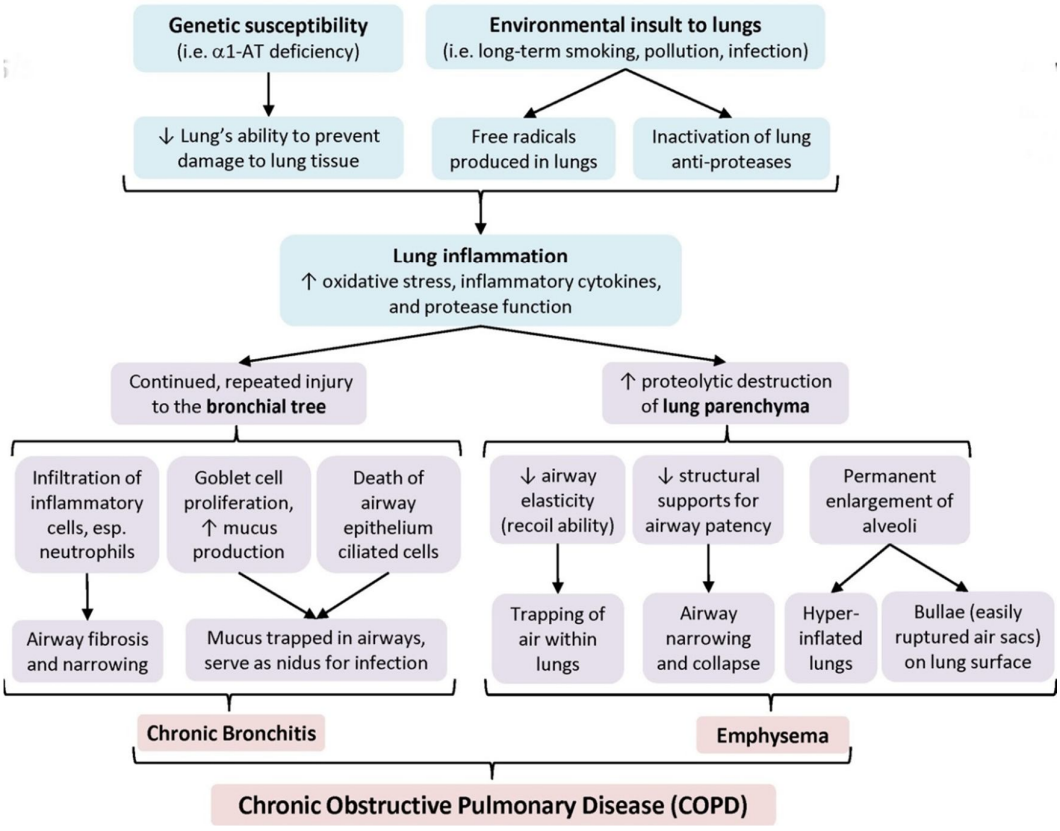


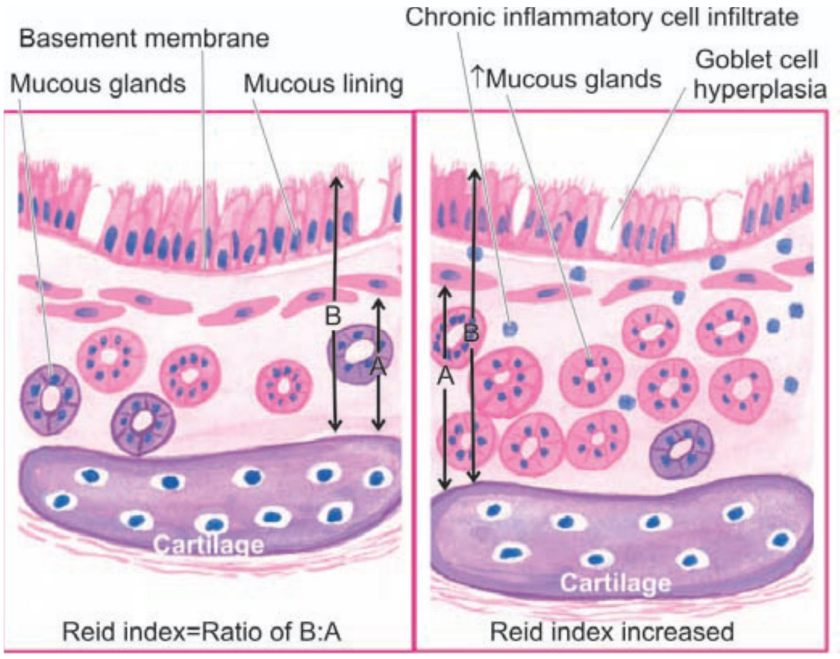
Fig No: 15- Pathogenic mechanism in COPD

Chronic bronchitis

MORPHOLOGIC FEATURES.

Gross*:* the walls of the bronchi will have increased thickness, hyperemic and edematous. Inside the lumen of bronchi and bronchioles mucus plugs and purulent exudate are present.

Microscopy: Reid index is used for the histological definition. Reid index is the ratio between width of the sub mucosal mucus producing glands (i.e. hypertrophy and hyperplasia) in the cartilage-containing large airways to that of the total bronchial wall.



normal **chronic bronchitis**

Fig No: 16- Reid index in Chronic bronchitis

Emphysema

Grossly*:* Voluminous lungs with, pale little blood. The edges are rounded. Enlargement of air spaces is seen in mild cases. Bullae and blebs are seen from the surface of lungs in progressed cases. The bullae (1 cm or more in diameter) are formed by the rupture of adjacent air spaces while blebs are formed by rupture of alveoli into the sub pleural space resulting in spontaneous pneumothorax.

Microscopy: Based on the different types of emphysema already mentioned, either respiratory bronchioles or alveolar ducts or alveolar sacs are dilated. Fibrosis are not found in bullae and blebs.

CLINICAL FEATURES OF COPD

Fig No: 17- Clinical features of COPD

The typical finding that occur in COPD patients are limitation in the expiratory flow which can't be fully reversed. The main symptoms the patient will be complaining are exertional dysponea, cough and

sputum production. It is usually seen that the symptoms will have a prolonged course and incremental over a tome period.

Cough

Cough and sputum production are usually the first symptoms, often termed as 'smoker's cough'. Usually the first symptom the patient will be telling is cough. Hemoptysis may be a complication of COPD but usually will not occur.

Shortness of breath

COPD expiratory airflow obstruction is typically not reversible. Typically the difficulty in breathing is more on exertion of a prolonged duration and increases over time.] In the advanced stages, even at rest be always present. Breathlessness results in anxiety and decreases COPD patients quality of life and makes the patient seek healthcare. The severity should be quantified by documenting the level exertion the patient can manage before stopping. Modified MRC dysponea scale is the current used scale to grade the dysponea.

Grading symptoms

Modified Medical Research Council (MMRC) dyspnea scale

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

Fig No: 18-Modified MRC Dysponea Scale

Core pulmonale was classically described as-"hypertrophy of right ventricle from pathology affecting function or lung structure". Pulmonary hypertension is the underling pathological mechanism in hypertrophy of right ventricle in cor pulmonale.

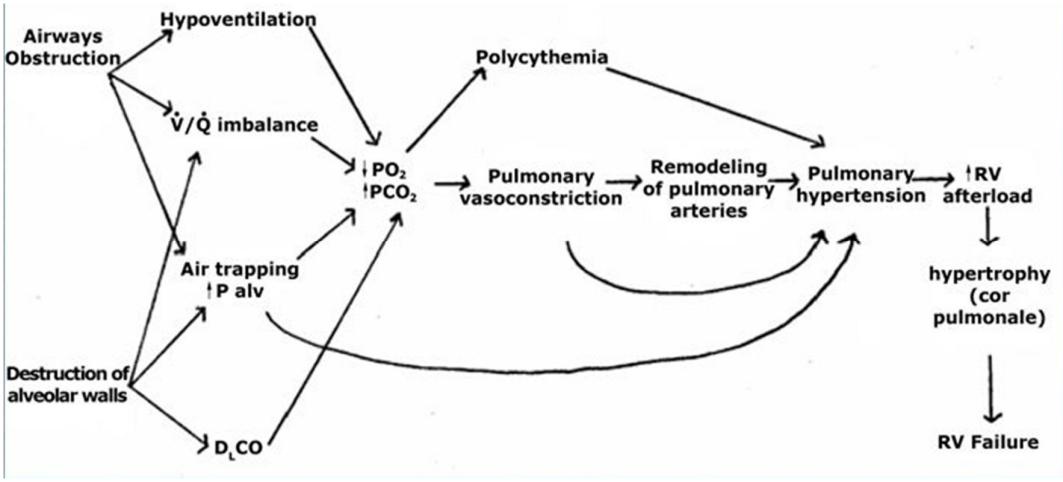


Fig No: 19- Mechanism Of Cor-pulmonale

Other features

In COPD, patient will be having more difficulty in exhaling out the air compared to inspiring. When obstruction or narrowing of air pathways associated with COPD is present, there will be musical quality sound called wheezing. Barrel shaped chest is typically described in advanced cases of COPD.

In more progressed cases of COPD, the pressure will be reflected back on the heart which will produce strain of right ventricle, and the same pressure is transmitted as raised jugular venous pulse. Usually clubbing is not a significant finding in COPD, but if a patient has clubbing underling malignancy should be ruled out.

COPD often associated with lot of systemic manifestations like metabolic disorders which includes diabetes mellitus, hypertension, obesity ,obstructive lung disorders, skeletal muscle wasting ,depression and anxiety etc.

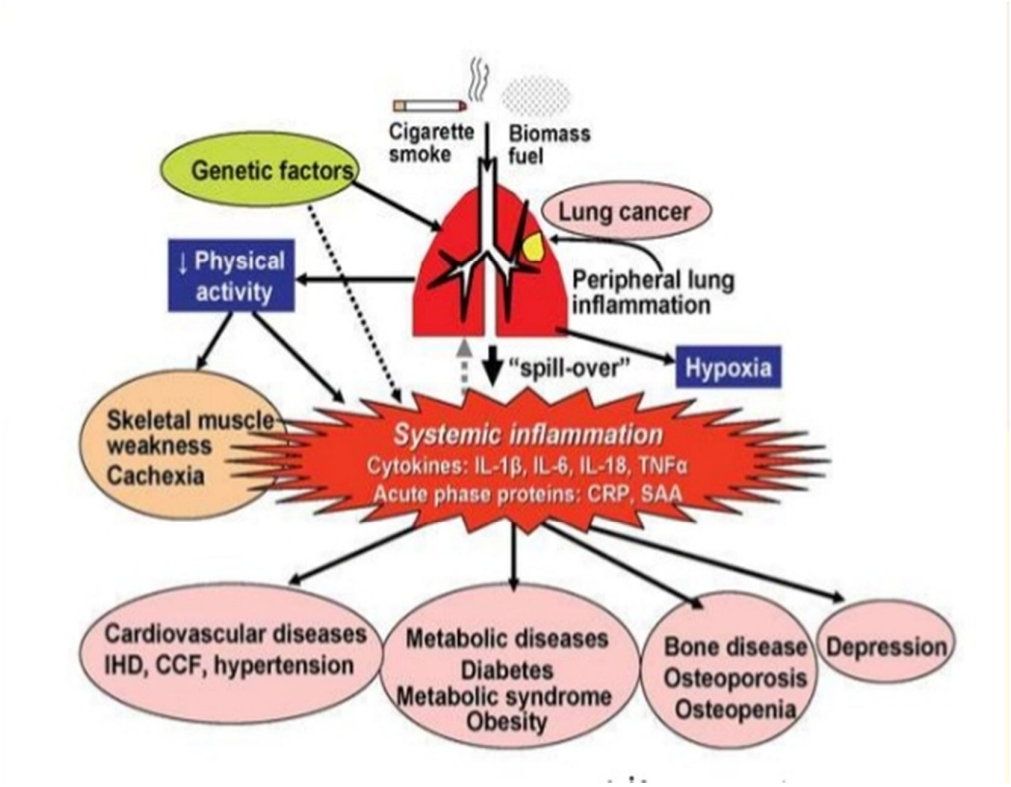


Fig No: 20- Systemic Manifestations of COPD

EXACERBATION

Acute exacerbations of COPD is the condition where there will be increased in breathlessness or increase in production of sputum or increase in cough and a change in color of the sputum produced. The patient who have acute exacerbations shows signs of more difficulty in breathing such as fast breathing, a fast heart rate, sweating or active use of muscles in neck and other accessory muscles, may be associated with bluish coloration of the skin along with mucosa. Patient may have confusion because of hypoxia. Wheezing and crepitation's are found in those patients.

Infectious (60-80% of all exacerbations)	Environmental factors
Frequent (70-85% of all infectious exacerbation)	Air pollution
Viruses (influenza and parainfluenza viruses, rhinoviruses, coronaviruses)	Non-adherence to respiratory medication
Hemophilus influenzae	Cold air
Streptococcus pneumoniae	Allergens
Moraxella catarrhalis	Tobacco smoking
Infrequent (15-30% of all infectious exacerbations)	
Pseudomonas aeruginosa	
Opportunistic gram-negative species	
Staphylococcus aureus	
Chlamydophila pneumoniae	
Mycoplasma pneumoniae	

Fig No: 21- Factors Causing Exacerbations

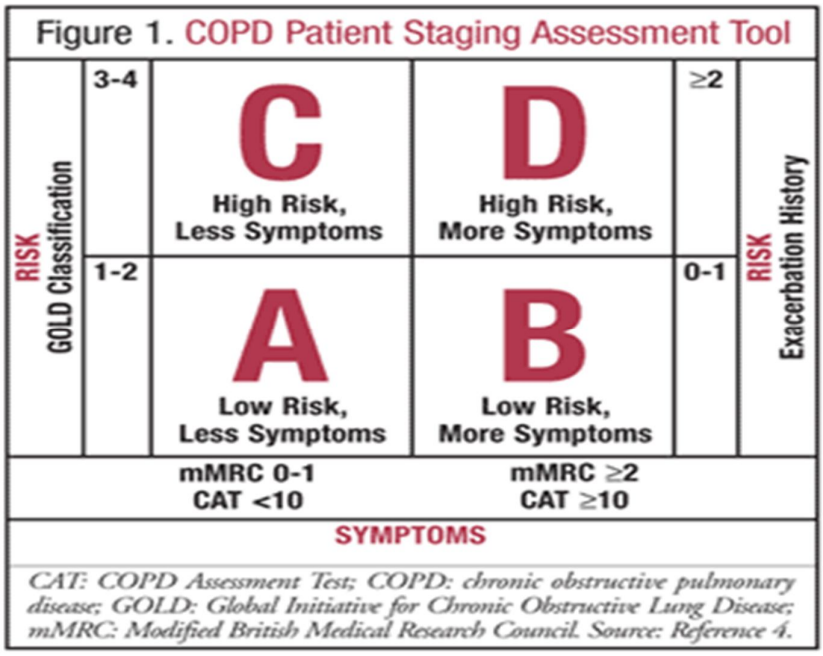


Fig No: 22-COPD Patient Staging Assessment Tool

INVESTIGATIONS

1) Pulmonary function testing

The diagnosis of COPD is confirmed by spirometry. It helps in diagnosing the same and also help to know the severity of the disease.

Fig No: 23- Pulmonary Function Test

The diagnosis of COPD is made when there is airflow limitation shown by post bronchodilator FEV1 < 80% and also FEV1/ FVC < 70. Peak flow can help in diagnosis of COPD, but it is not specific, because it is only affected in later stages of COPD, so better to use is the ratio of FEV1/FVC

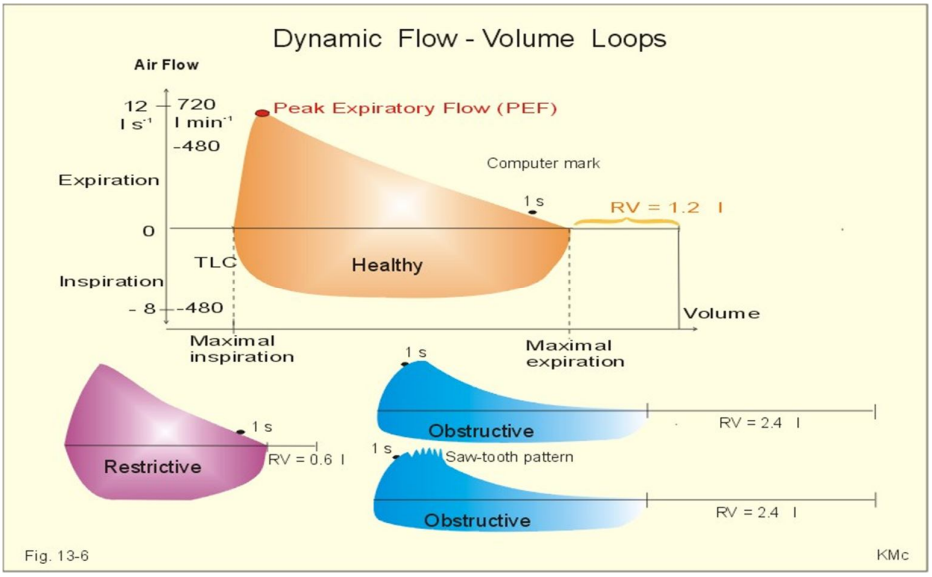


Fig No: 24-Dynamic Flow Volume Loops

PROGNOSIS

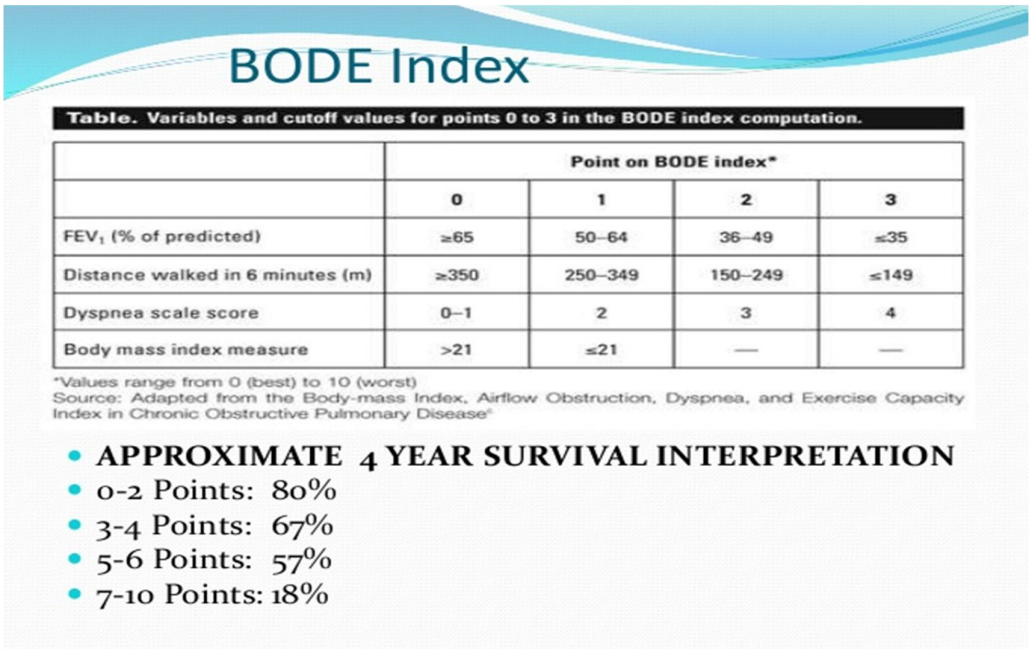


Fig No:25- BODE Index

By the help of BODE index we can tell the prognosis of COPD patients, their 4 year survival percentage and its components include exercise capacity, body mass index, dyspnea on MMRC scale and what distance the patient can walk by 6 minute's. It is a good prognostic grading and predict death and early hospitalization.

2) Chest X- ray

A plain Chest X-Ray posterio-anterior view and lateral view are done

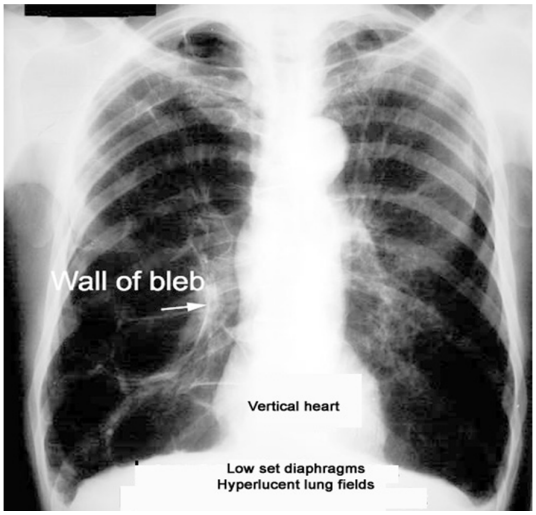


Fig No: 26-Chest X Ray

Emphysema can be diagnosed in chest X-Ray if there is two out of five criteria

1. The space between anterior heart wall and sternum that is the retrosternal space more than 2.54 cm measured in lateral view

2. Hyper-lucency of lung fields in X ray

3. Flat and low diaphragm on lateral view

4. Flat and low diaphragm on PA view

5. Clear walled lesions or Bullae seen.

3) Blood count

A blood count is useful to find out polycythemia or anemia in patients.

4) ABG and pulse oximetry

Arterial blood gas analysis helps to find out the hypoxemic status of the blood.

Pulse oximetry is a simple and bed side investigation which help to find out the oxygen saturation and help to intervene the patient as early as possible.

5) α1-antiproteinase

the enzyme deficiency is investigated usually in young patients predominantly present as emphysema.

6) Helium dilution technique and body plethismography.

These tests are not routinely done help to asses the hyper inflation and body pletismography will help to find out volumes especially in COPD patients having bullae.

7) Exercise tests

Exercise tests help to find out the exercise tolerance of the patients and also help to judge the patients responding to rehabilitation therapy.

8) HRCT

HRCT is the main investigation in assessing COPD patients, It helps to detect the disease at earlier stage compared to X rays and other investigations so that as as to intervene as early as possible especially in emphysema

MANAGEMENT

TREATMENT GOALS OF A COPD PATIENT

Reduction in current symptoms
Relief in breathlessness and other symptoms
Improvement in exercise tolerance
Improvement in overall health-related quality of life
Reduction of future risk
Prevention (or slowing down) of disease progression
Prevention of disease exacerbations
Reduction in disease-related mortality
Minimizing adverse effects from treatment

NON – PHARMACOLOGICAL METHODS

- **SMOKING CESSATION**
- **LONG TERM OXYGEN THERAPY**
- **PULMONARY REHABILITATION**
- **NON INVASIVE VENTILATION**
- **SURGERY**

SMOKING CESSATION: It is considered as the prime most important step to prevent further progression of COPD and decrease its exacerbations.

Fig No: 27- Smoking Cessation Nicotine Replacement Therapy

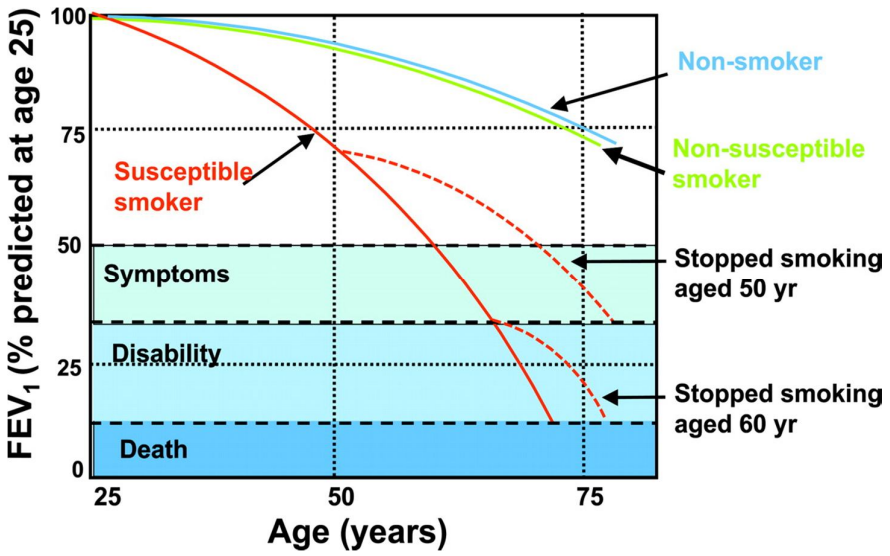


Fig No:28- FEV1 prediction with smoking cessation

OXYGEN THERAPY

Long term oxygen therapy is one of the important benefited treatment in COPD patients who are having more severe COPD. Improves quality of life.

INDICATIONS

Continuous use of oxygen	Intermittent use of oxygen
Resting Pao2 ≤ 55 mm Hg Resting Pao2 of 56-59 mm Hg with any one of the following Edema suggestive of CCF P pulmonale in ECG increased RBC (hematocrit, > 56%)	desaturation with exercise<88% desaturation at night <88%

PULMONARY REHABILITATION THERAPY

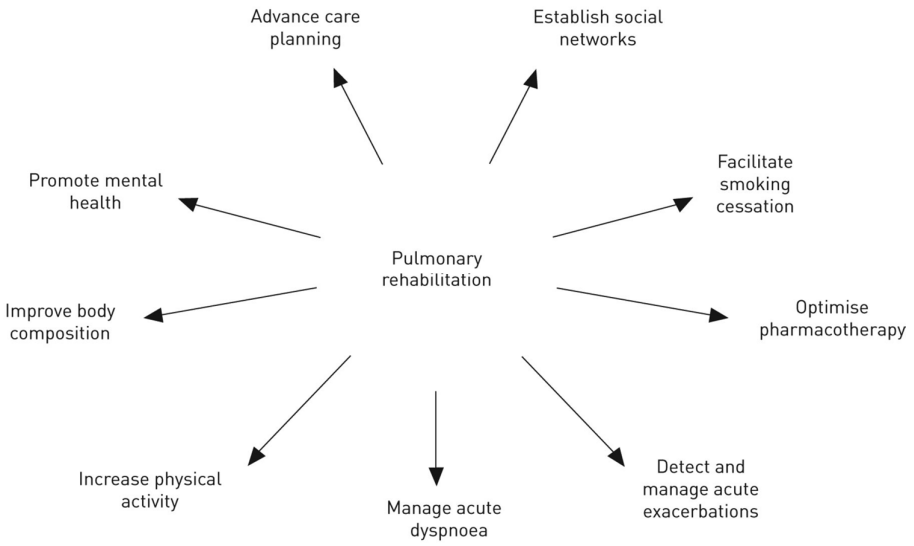


Fig No: 29- Pulmonary Rehabilitation Therapy

NON INVASIVE VENTILATION

- Mainly used in acute exacerbation states, the main advantage of the following is that it will increase the inspiratory pressure helping in more gas exchange

VACCINATION STRATEGIES

Influence and pneumococcal vaccinations are given especially who have recurrent exacerbations in order to decrease the number of exacerbations.

SURGERIES

1) Bullectomy- large bullae excised to prevent airflow limitation

2) Lung volume reduction surgery (LVRS)-upper lobe emphysema, with preserved gas transfer and no evidence of pulmonary hypertension, may benefit

3) Lung transplantation

This modality considered in advanced disease ; FEV1 <35% (PaO_2 < 60 mmHg and $PaCO_2$ > 50 mmHg).

PHARMACOLOGICAL MANAGEMENT

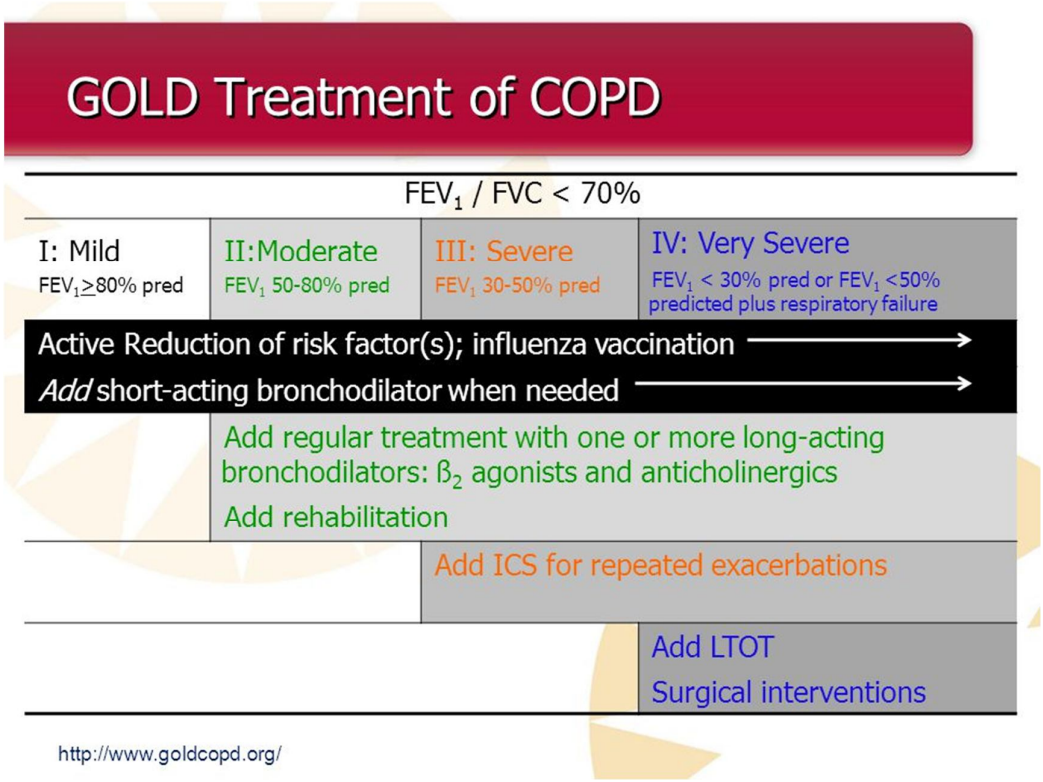


Fig No: 30- Gold Strategy in treating COPD

Mild COPD	Moderate COPD	Moderate to severe COPD	Severe to very severe COPD
• If patient has persistent symptoms, treat with short-acting bronchodilators around the clock (e.g., ipratroprium and salbutamol inhalation • If the symptoms are periodic, treat on an as-needed basis (e.g., salbutamol inhalation • Counsel for smoking cessation and ensure patient has appropriate vaccinations.	• Treat with long-acting bronchodilators around the clock (e.g., $ß_2$ agonist such as salmeterol and formoterol, or anticholinergic agent such as tiotropium) for symptomatic relief. • Counsel for smoking cessation and ensure patient has appropriate vaccinations.	• Treat with a long-acting bronchodilator combined with an inhaled corticosteroid (e.g., salmeterol/fluticasone 500 mcg, b.i.d., or formoterol/budesonide 400 mcg, b.i.d.) for prevention of exacerbations and improvement in symptoms. • Counsel for smoking cessation and ensure patient has appropriate vaccinations.	• Treat with tiotropium and a long-acting $ß_2$ agonist/ inhaled corticosteroid combination to provide maximal relief of symptoms and reduce risk of exacerbation. • Counsel for smoking cessation and ensure patient has appropriate vaccinations.

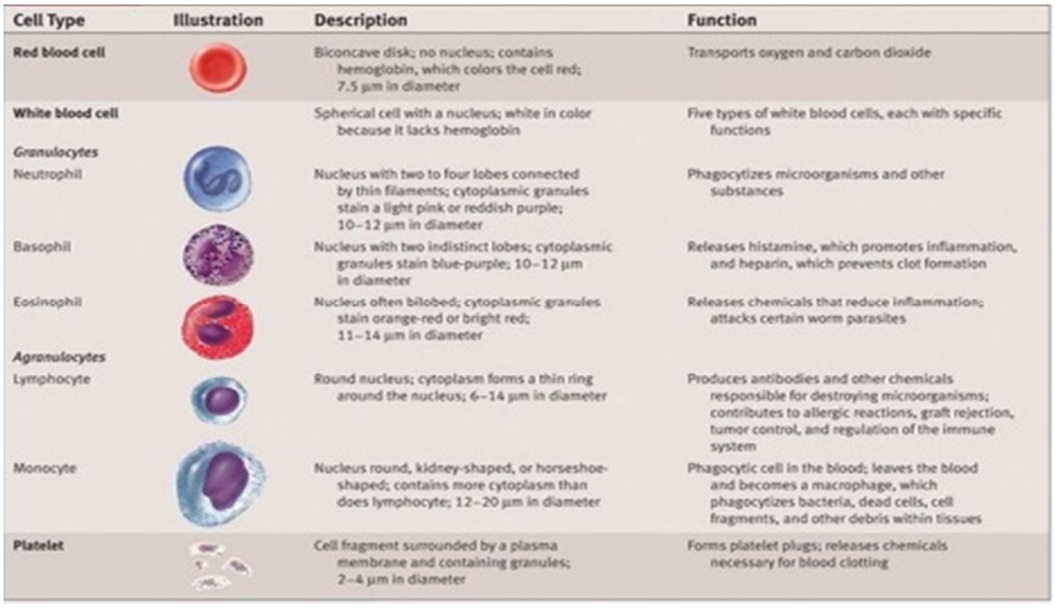
Fig No: 31- Treatment Options in COPD

Mild COPD: Add short acting β2-agonists Fenoterol / Salbutamol / Terbutaline.

Moderate COPD: Add one or more long acting bronchodilators such as Formterol/ Salmeterol and if needed add either short acting(Ipratropium bromide/ Oxitropium bromide) or long acting (Tiotropium) anticholinergics.

Severe COPD: Add inhaled steroids (Budesonide / Fluticasone/ Triamcinolone and if the response is not satisfactory, systemic steroids(Prednisone/ Methyl-prednisolone).

NEUTROPHIL LYMPHOCYTE RATIO(NLR)



Cell Type	Illustration	Description	Function
Red blood cell		Biconcave disk; no nucleus; contains hemoglobin, which colors the cell red; 7.5 µm in diameter	Transports oxygen and carbon dioxide
White blood cell		Spherical cell with a nucleus; white in color because it lacks hemoglobin	Five types of white blood cells, each with specific functions
Granulocytes			
Neutrophil		Nucleus with two to four lobes connected by thin filaments; cytoplasmic granules stain a light pink or reddish purple; 10–12 µm in diameter	Phagocytizes microorganisms and other substances
Basophil		Nucleus with two indistinct lobes; cytoplasmic granules stain blue-purple; 10–12 µm in diameter	Releases histamine, which promotes inflammation, and heparin, which prevents clot formation
Eosinophil		Nucleus often bilobed; cytoplasmic granules stain orange-red or bright red; 11–14 µm in diameter	Releases chemicals that reduce inflammation; attacks certain worm parasites
Agranulocytes			
Lymphocyte		Round nucleus; cytoplasm forms a thin ring around the nucleus; 6–14 µm in diameter	Produces antibodies and other chemicals responsible for destroying microorganisms; contributes to allergic reactions, graft rejection, tumor control, and regulation of the immune system
Monocyte		Nucleus round, kidney-shaped, or horseshoe-shaped; contains more cytoplasm than does lymphocyte; 12–20 µm in diameter	Phagocytic cell in the blood; leaves the blood and becomes a macrophage, which phagocytizes bacteria, dead cells, cell fragments, and other debris within tissues
Platelet		Cell fragment surrounded by a plasma membrane and containing granules; 2–4 µm in diameter	Forms platelet plugs; releases chemicals necessary for blood clotting

Fig no:32- Blood Cells

Normal differential leucocyte count

Neutrophils	40-75%
Basophils	<1-2%
Eosinophils	2-6%
Lymphocytes	20-40%
Monocytes	2-8%

The neutrophil to lymphocyte ratio (NLR), is a simple ratio that is obtained from the complete blood count of patient, which is found out by dividing absolute neutrophil count as numerator and absolute lymphocyte count as the denominator. So any conditions which alters the counts will change the ratio, which can increase or decrease. The ratio indicates the inflammatory status of the individual, that is the cellular mediated inflammatory response. High value of the ratio indicates there is some response to inflammation happening in the body. So many of the conditions NLR can vary and its value can be used in monitoring as a biomarker in those conditions, some are hypertension, diabetes, obesity, metabolic syndromes, cardiovascular disease, renal failure, any chronic malnutrition states, cerebrovascular disease, alzheimer's, COPD, and even in psychiatric conditions like delirium etc. This parameter can also used in various cancers monitoring of therapy of drugs, prognosis of

treatment with various therapies. The usefulness of NLR as an inflammatory marker can compared to other routinely used inflammatory markers like C-reactive protein interleukin-1, tumor necrosis factor-α, ESR etc.

Recently, it has been found that the use of NLR in various cancer prognostication including breast cancer, esophageal cancer, pancreatic cancer, colorectal cancers an elevated preoperative or pretreatment NLR, calculated from peripheral blood tests, was identified as an independent and readily available prognostic biomarker related to poor survival in numerous cancers, including colorectal cancer, breast cancer, gastric cancer and esophageal cancer, renal cell carcinomas and various study's are undergoing in evaluating the same as inflammation is a basic pathogenesis happening in all cancers and in those states the NLR values are altered.

NLR is a tool which helps to find out the severity of disease and also the activity status of the disease in COPD patients.

Significance of NLR:

(1) NLR levels are related to FEV1 by inverse relationship as NLR increases FEV1 decrease.

(2) COPD exacerbations can be predicted with NLR, and if NLR is more in routinely followed patients we can say the chances of future exacerbations are more.

(3) The severity of the exacerbation state can be said by the NLR value with out the help of spirometry.

(4) NLR can also predict the prognosis of the COPD patient by comparing it with the BODE index.

In COPD there will be continuous inflammatory process happening in the airways and also in the lung tissues. Now a days COPD is thought to be a systemic inflammatory disease, as result of that the levels of inflammatory markers which are in blood will be high compared to normal subjects. It has been found out that even in normal states in COPD patients the inflammatory marker levels will be high than in healthy subjects, and higher the markers higher the chances that patient can get future exacerbations.

IT has been well accepted for the elevation of WBC and neutrophils in COPD.COPD patients who had increased inflammatory markers like CRP, fibrinogen with increased WBC count has greater chances of getting co morbid conditions like pneumonia, diabetes, lung cancer, CAHD etc. Those who have frequent exacerbations have elevated

WBC counts in their blood picture and there raised value is a predictor of mortality. Elevated WBC and neutrophil counts were independently and significantly associated with mortality. Lymphopenia is also associate with poor prognosis and out come especially in acute infectious states like sepsis or bacteremia in COPD patients. So there comes the role of NLR which consists of both the things in which increased neutrophil count indicates activity of inflammation and decreased lymphocyte count shows poor general condition and the incompetence of immune system. So combing the factors NLR and the spirometry especially FEV1 helps to predict the future exacerbations of COPD and also with rise in NLR values the exercise capacity of the patient decreases. So everything adds to the fact that NLR reflects the severity and helps to monitor the same.

The mechanism of what happens in acute exacerbations explain the relationship of NLR and disease severity, as increased neutrophils in lung will cause the release of many of proteolytic enzymes from its granules like elastase matrix metalloproteases which are considered as culprits in emphysema. So it can be find that airway neutrophilia is inversely related to the lung function.

MATERIALS AND METHODS

Source of Study

The study is conducted on patients attending Coimbatore Medical College Hospital, Coimbatore during the study period (July 2016 to June 2017). A sum total of 100 patients with Chronic Obstructive Pulmonary Disease attending Coimbatore Medical College Hospital was included in the study, based on the inclusion and exclusion criteria. The study is done after getting informed signed consent from the patients participated in the same. Duration of study was one year.

Design of Study- Cross Sectional Study

Methods of Collection of Data

Sample Size-100 patients

Sampling Method: Random sampling

The study included patients with Chronic Obstructive Pulmonary Disease irrespective of the severity and duration of disease. Study cases are personally interviewed to get relevant details after getting informed signed consent. Based upon inclusion and exclusion criteria a minimum of 100 cases are selected. An exacerbation of COPD is defined as an

onset or worsening of more than two respiratory symptoms (ie, dyspnea, cough or wheeze, sputum amount or purulence) for two or more consecutive days.

Inclusion criteria

Stable diagnosed COPD patients of age 40 years or older who were current or ex smokers based on clinical history and examination attending Coimbatore Medical College Hospital.

Exclusion criteria

- age < 40 years
- Patients with and diagnosed as Bronchial Asthma, Bronchiectasis or Bullous lung disorders.
- Patients with active pulmonary tuberculosis.
- Patients with malignancy.
- Patients with hepatic disease, renal disease, myocardial infaction.
- Patients with any other acute or chronic infections.
- Patients with pneumonia.
- Patients with dementia.

- Patients with Diabetes Mellitus.
- Patients receiving systemic corticosteroids, antibiotics.
- Patients receiving immunosuppressive treatment.

Methods of study:

Data is collected using pretest proformas according to the objectives of the study. After getting informed signed consent detailed history and examination were done in 100 patients included in the study. The aim and purpose of study was was informed to the patients and there informed consent obtained.

Those patients who satisfied all the inclusion and exclusion criteria were selected for the study

INVESTIGATIONS

1.ROUTINE COMPLETE BLOOD COUNT

TC, DC (including neutrophil and lymphocyte counts), Hemoglobin percentage.

2.BLOOD BIOCHEMISTRY

Random blood sugar

Blood urea

Serum creatinine

Serum electrolytes: Sodium, Potassium

3.ECG

4.IMAGING STUDIES

CT Chest

Chest X ray PA view

5.PULMONARY FUNCTION TEST

6.sputum AFB, sputum culture and sensitivity (if needed)

STATISTCAL METHODS

All the dates were entered in a data collection sheet in an Excel format and analysed using SPSS Software. Numerical values were reported using mean and standard deviation or median. Categorical values are reported using number and percentages. Probability value (p) value less than 0.05 was considered a statistically significant

RESULTS

TABLE NO: 1: AGE DISTRIBUTION

AGE IN YEARS	NO OF PATIENTS	PERCENTAGE
< 50	9	9%
51-60	31	31%
61-70	48	48%
>70	12	12%

CHART NO: 1- AGE DISTRIBUTION

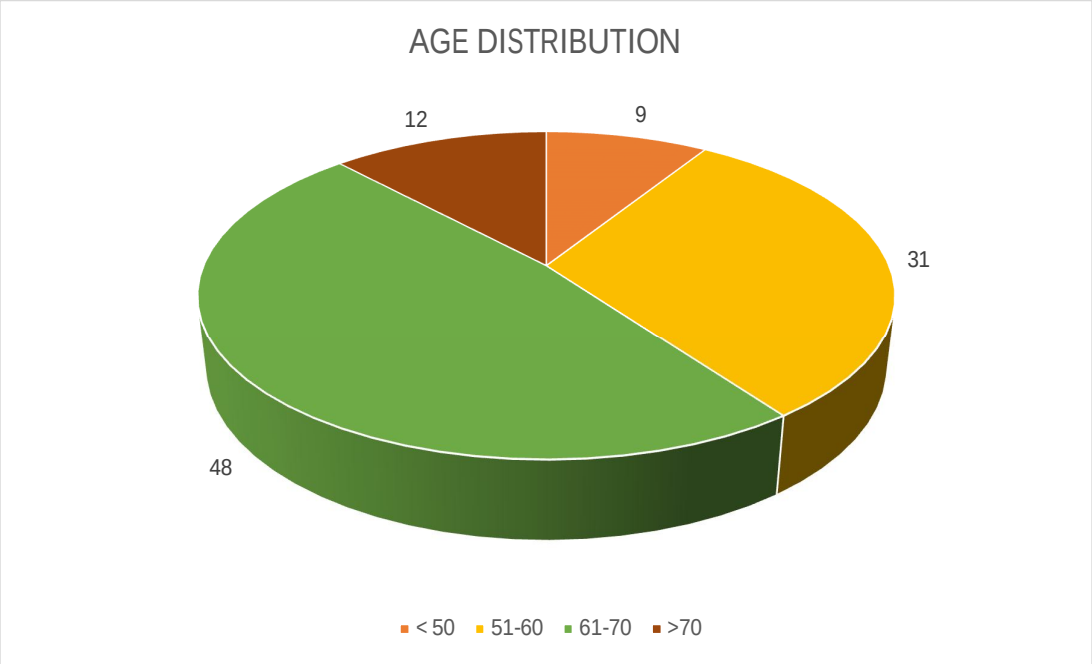


TABLE NO: 2: AGE DISTRIBUTION VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

AGE IN YEARS	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
< 50	4.08	1.34
51-60	3.87	1.79
61-70	3.7	1.47
>70	4.15	1.44
P VALUE - 0.784		
NON SIGNIFICANT		
ANOVA		

CHART NO: 2: AGE DISTRIBUTION VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

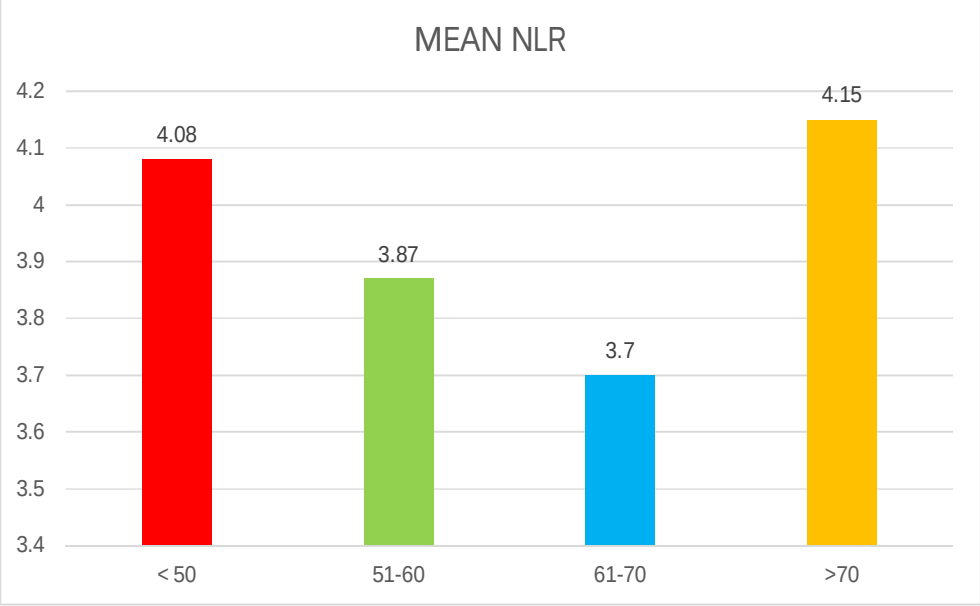


TABLE NO: 3: SEX DISTRIBUTION

SEX	NO OF PATIENTS	PERCENTAGE
MALE	91	91%
FEMALE	9	9%

CHART NO: 3: SEX DISTRIBUTION

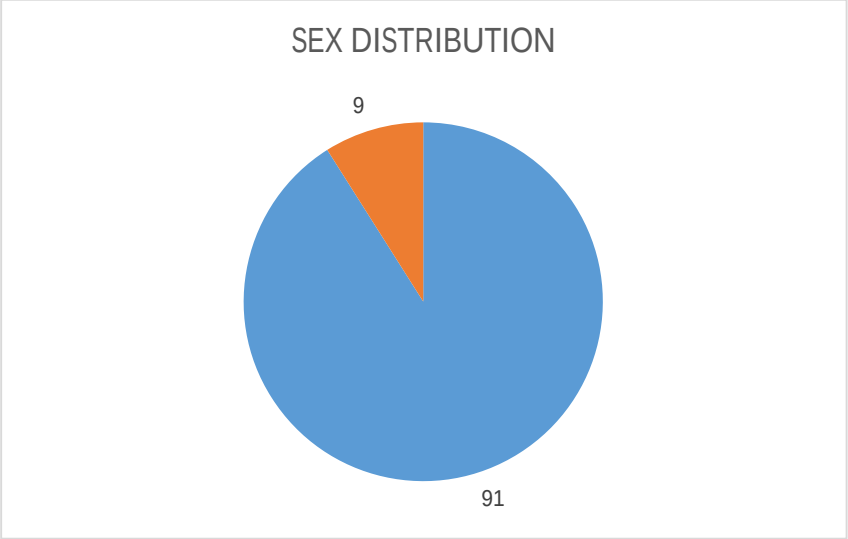


TABLE NO: 4- SEX DISTRIBUTION VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

SEX	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
MALE	3.83	1.55
FEMALE	3.87	1.65
P VALUE - 0.922		
NON SIGNIFICANT		
UNPAIRED T TEST		

TABLE NO: 5-DURATION OF YEARS OF COPD

DURATION	NO OF PATIENTS	PERCENTAGE
< 5 YEARS	30	30%
5-10 YEARS	24	24%
> 10 YEARS	46	46%

CHART NO: 4-DURATION OF YEARS OF COPD

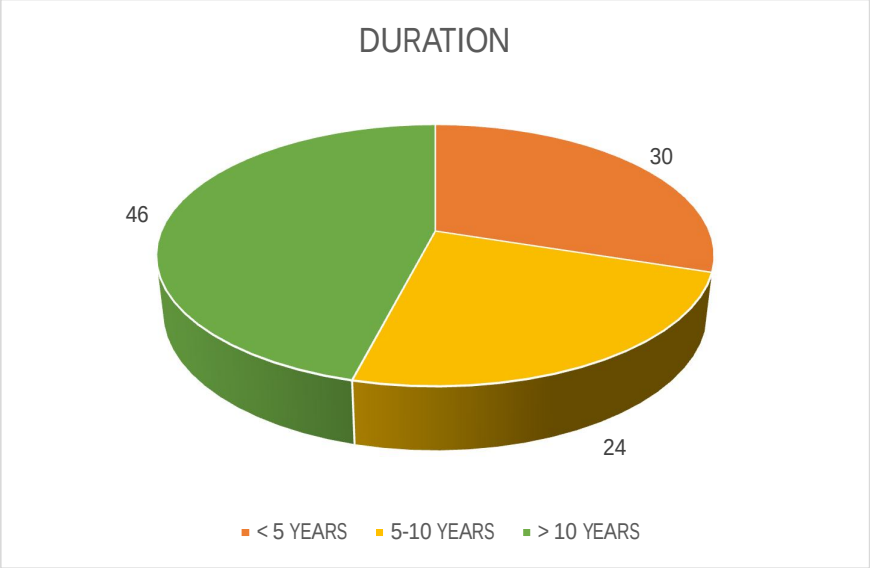


TABLE NO:6- DURATION OF ILLNESS VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

DURATION	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
< 5 YEARS	2.78	1.47
5-10 YEARS	3.99	1.48
> 10 YEARS	4.45	1.28
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

CHART NO:5-DURATION OF YEARS VS MEAN NLR

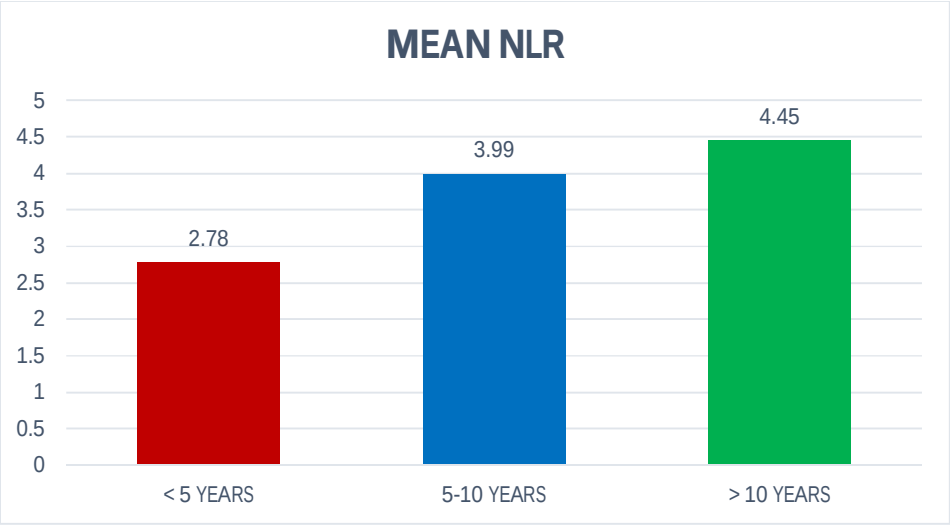


TABLE NO:7-SMOKING STATUS OF PATIENTS

SMOKING	NO OF PATIENTS	PERCENTAGE
YES	68	68%
NO	32	32%

CHART NO:6-SMOKING STATUS OF PATIENTS

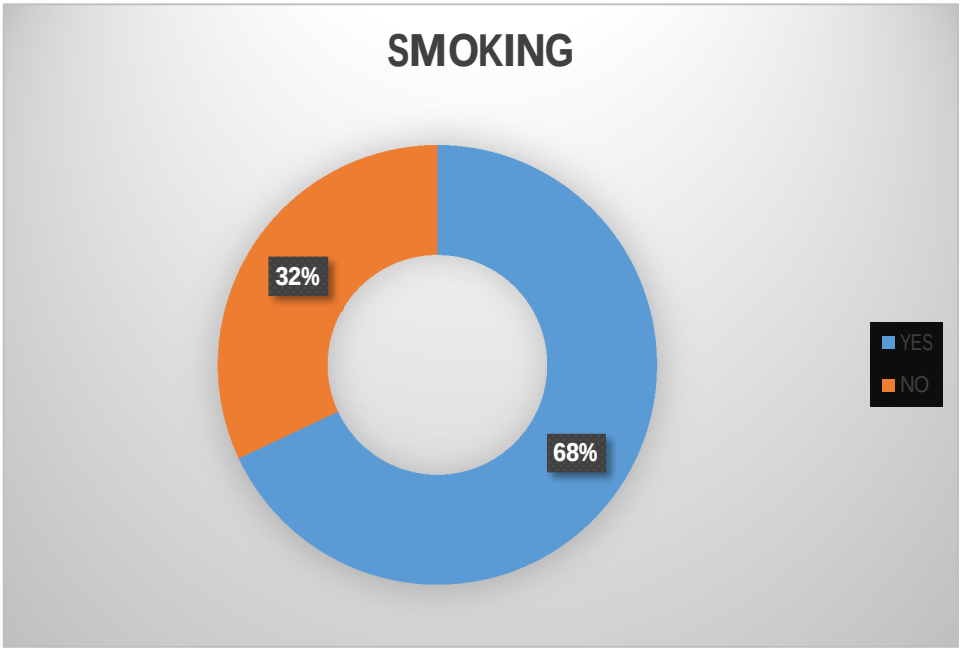


TABLE NO:8- SMOKING STATUS VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

SMOKING	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
YES	4.38	1.37
NO	2.69	1.27
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO:7- SMOKING STATUS VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

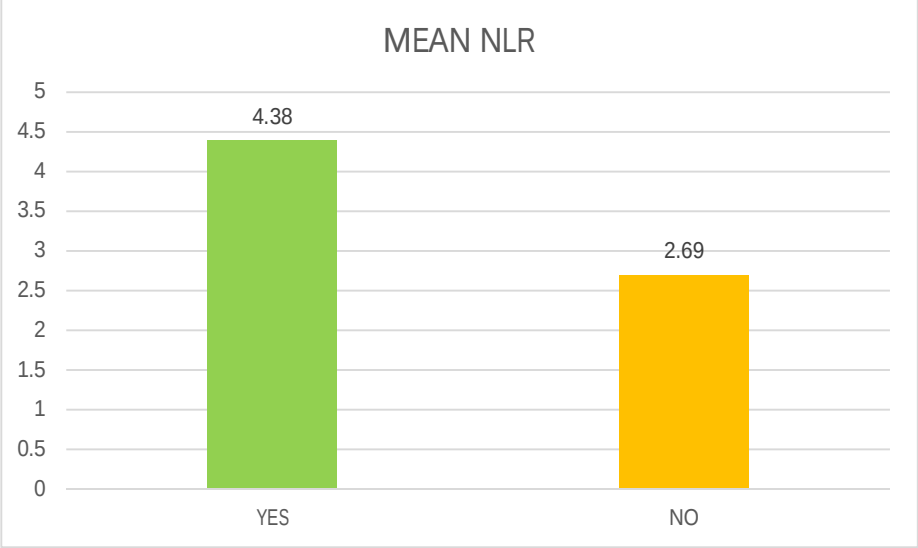


TABLE NO:9-EXPOSURE TO BIOMASS FUEL

BIOMASS FUEL	NO OF PATIENTS	PERCENTAGE
YES	52	52%
NO	48	48%

CHART NO:8 -EXPOSURE TO BIOMASS FUEL

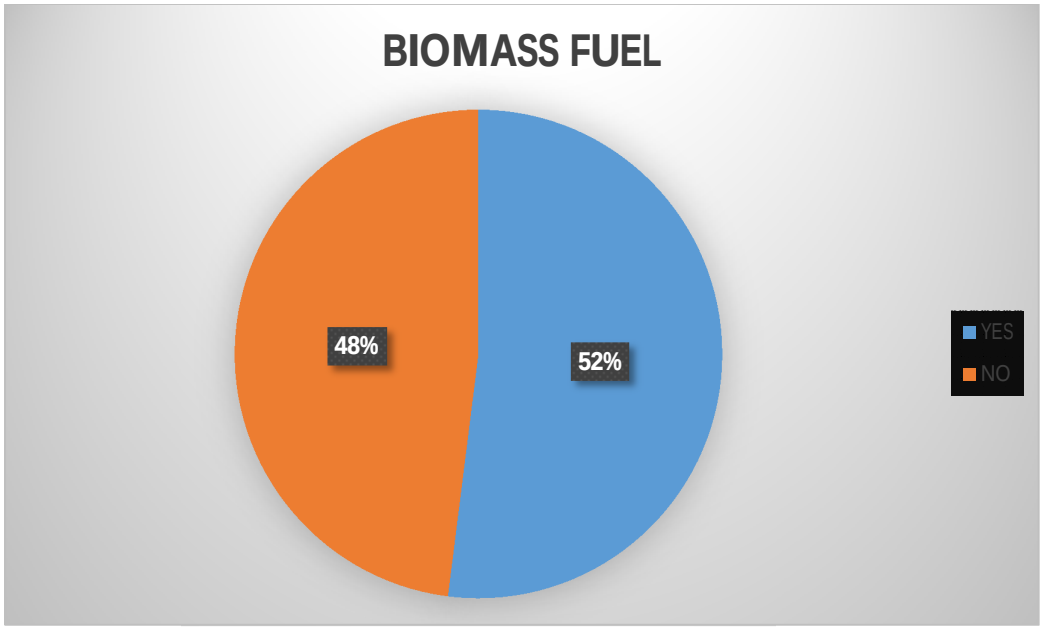


TABLE NO:10- BIOMASS FUEL EXPOSURE VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

BIOMASS FUEL	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
YES	4.25	1.54
NO	3.39	1.45
P VALUE - 0.005		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO:9- BIOMASS FUEL EXPOSURE VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

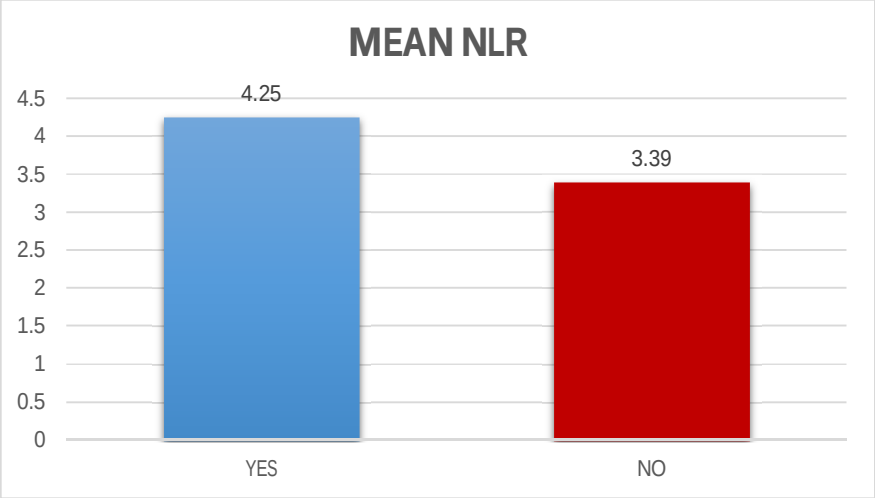


TABLE NO: 11- ENVIRONMENTAL EXPOSURE

ENVIRONMENTAL EXPOSURE	NO OF PATIENTS	PERCENTAGE
YES	56	56%
NO	44	44%

CHART NO: 10- ENVIRONMENTAL EXPOSURE

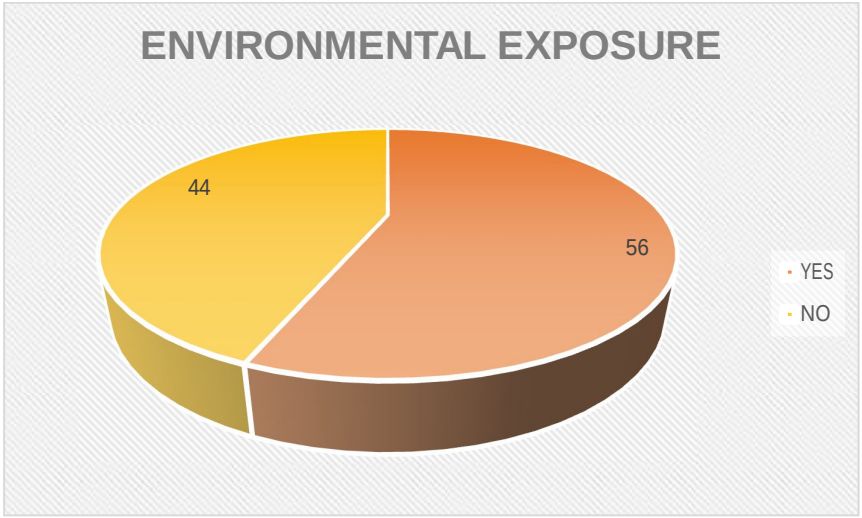


TABLE NO: 12- ENVIRONMENTAL EXPOSURE VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

ENVIRONMENTAL EXPOSURE	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
YES	4.12	1.57
NO	3.48	1.46
P VALUE - 0.043		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO: 11- ENVIRONMENTAL EXPOSURE VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

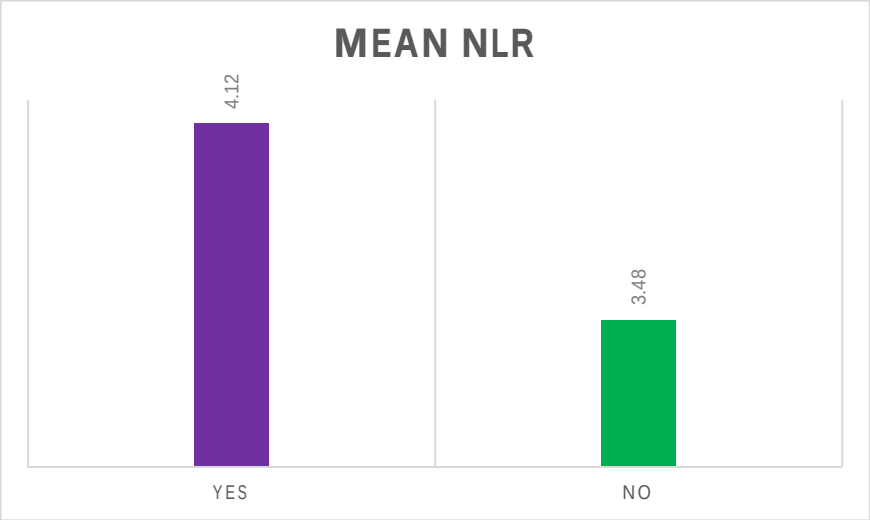


TABLE NO: 13- HYPERTENSION PATIENTS

HYPERTENSION	NO OF PATIENTS	PERCENTAGE
PRESENT	36	36%
ABSENT	64	64%

CHART NO: 12- HYPERTENSION PATIENTS

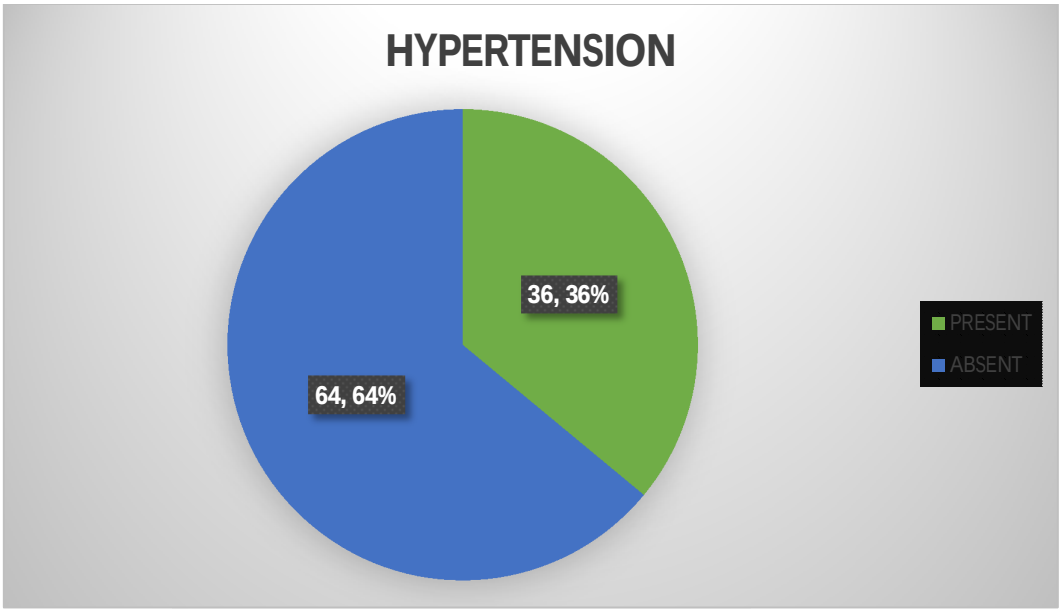


TABLE NO: 14- HYPERTENSION VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

HYPERTENSION	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
PRESENT	4.16	1.67
ABSENT	3.66	1.46
P VALUE - 0.119		
NON SIGNIFICANT		
UNPAIRED T TEST		

CHART NO: 13- HYPERTENSION VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

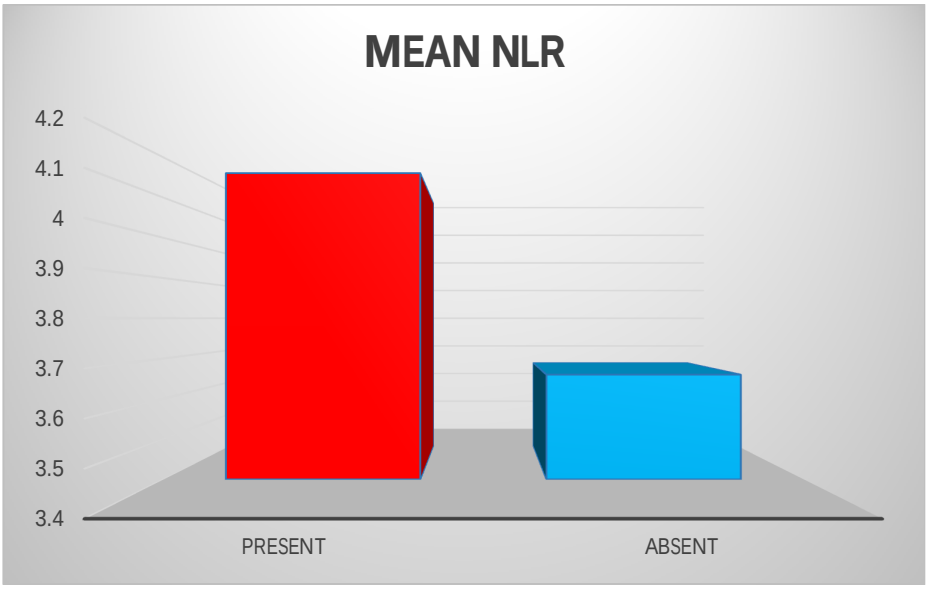


TABLE NO:15- PLACE OF PATIENTS

PLACE	NO OF PATIENTS	PERCENTAGE
URBAN	39	39%
RURAL	61	61%

CHART NO:14- PLACE OF PATIENTS

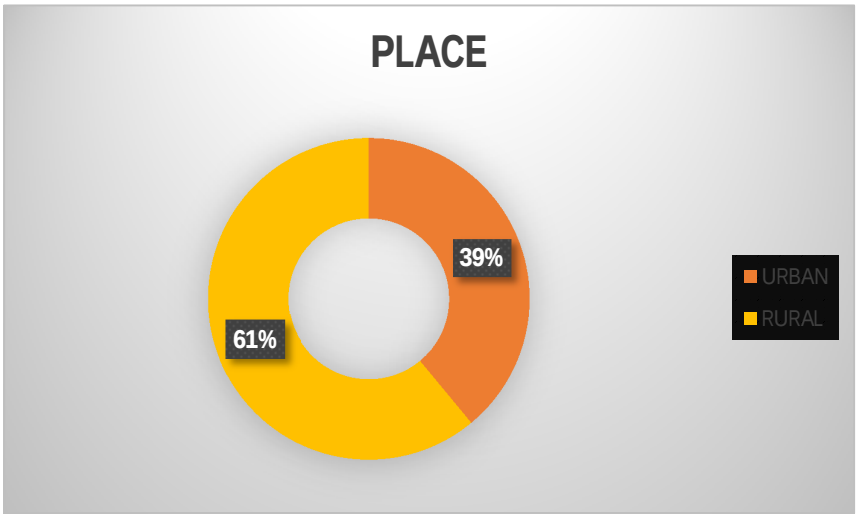


TABLE NO: 16- PLACE OF ORIGIN OF PATIENTS VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

PLACE	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
URBAN	3.72	1.64
RURAL	3.91	1.5
P VALUE - 0.558		
NON SIGNIFICANT		
UNPAIRED T TEST		

CHART NO: 15- PLACE OF ORIGIN OF PATIENTS VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

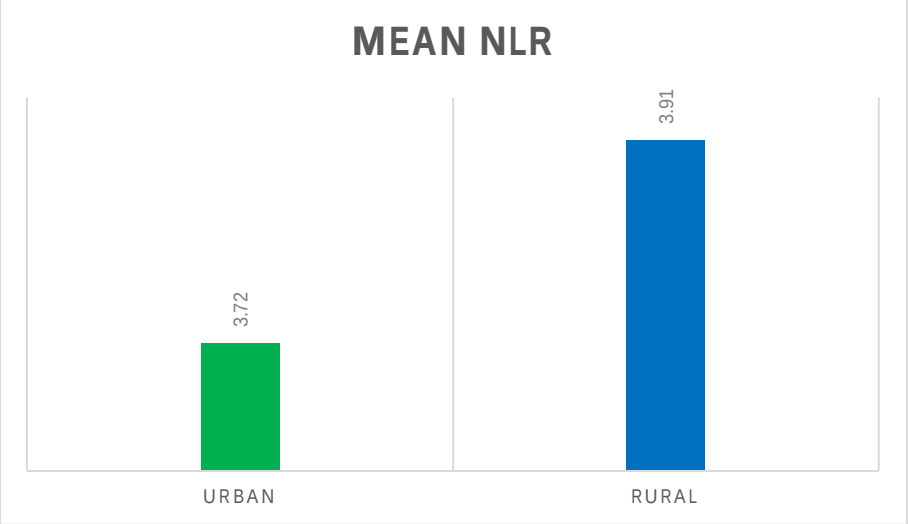


TABLE NO: 17- MMRC GRADING OF DYSPONEA OF PATIENTS

MMRC GRADING	NO OF PATIENTS	PERCENTAGE
GRADE 1	12	12%
GRADE 2	26	26%
GRADE 3	49	49%
GRADE 4	13	13%

CHART NO: 16- MMRC GRADING OF DYSPONEA OF PATIENTS

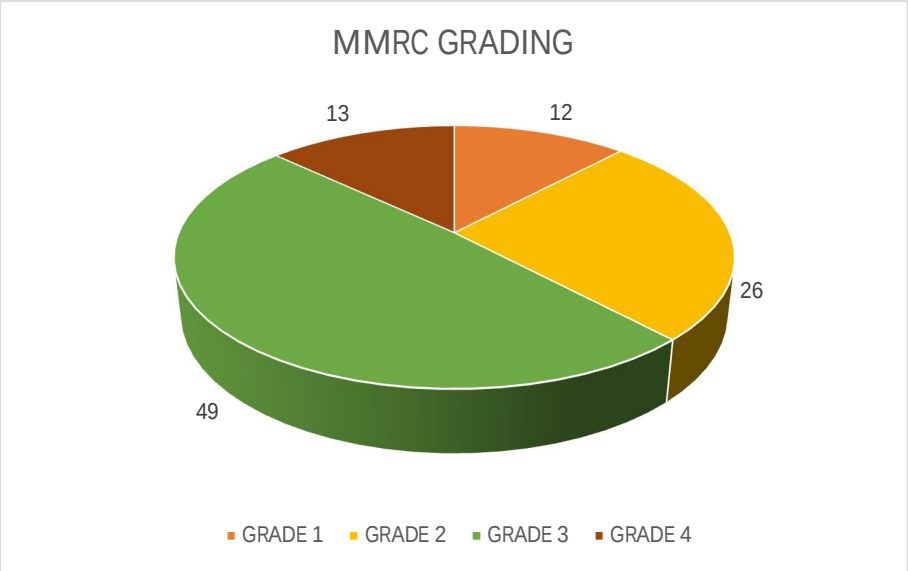


TABLE NO:18- MMRC GRADING VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

MMRC GRADING	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
GRADE 1	1.98	0.48
GRADE 2	2.52	0.98
GRADE 3	4.74	1.17
GRADE 4	4.8	0.77
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

CHART NO:17- MMRC GRADING VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

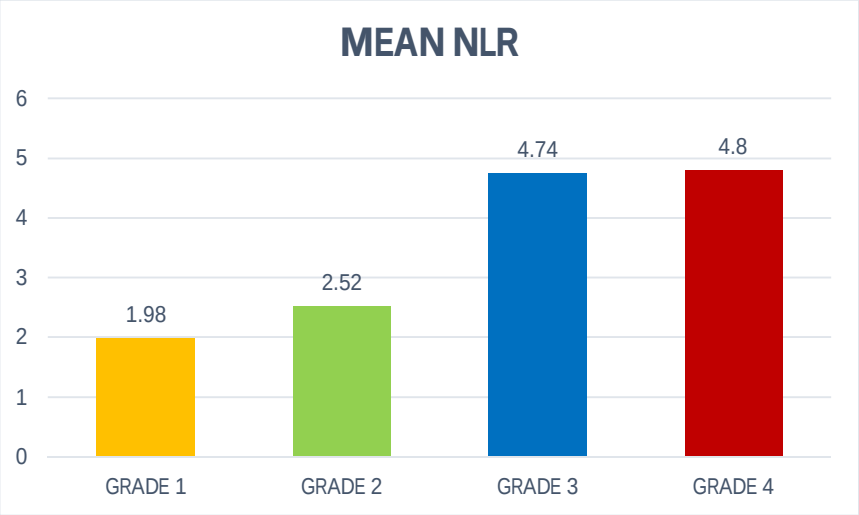


TABLE NO :19- FEV1 OF PATIENTS

FEV1	NO OF PATIENTS	PERCENTAGE
MILD	12	12%
MODERATE	30	30%
SEVERE	15	15%
VERY SEVERE	43	43%

CHART NO :18- FEV1 OF PATIENTS

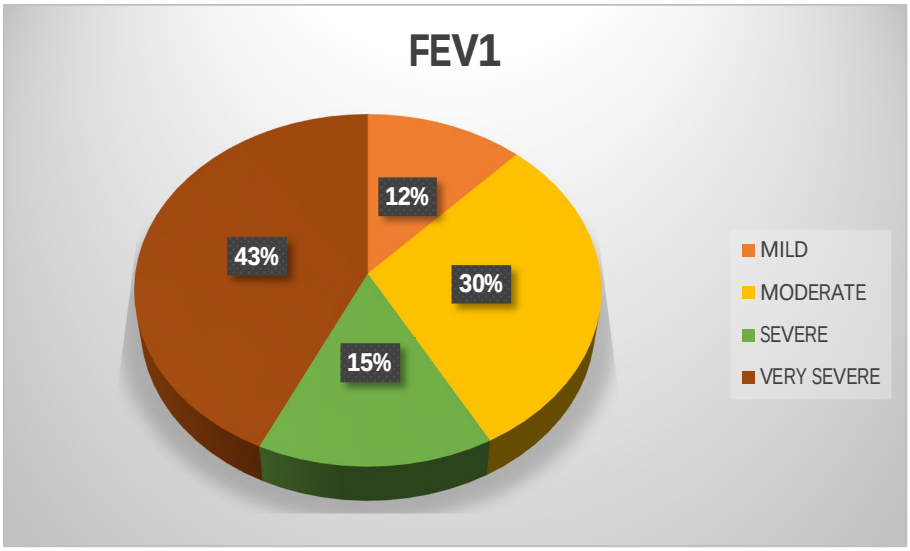


TABLE NO:20-FEV1 VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

FEV1	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
MILD	2.09	0.65
MODERATE	2.59	1.04
SEVERE	4.38	1.35
VERY SEVERE	5.01	0.84
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

CHART NO:19-FEV1 VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

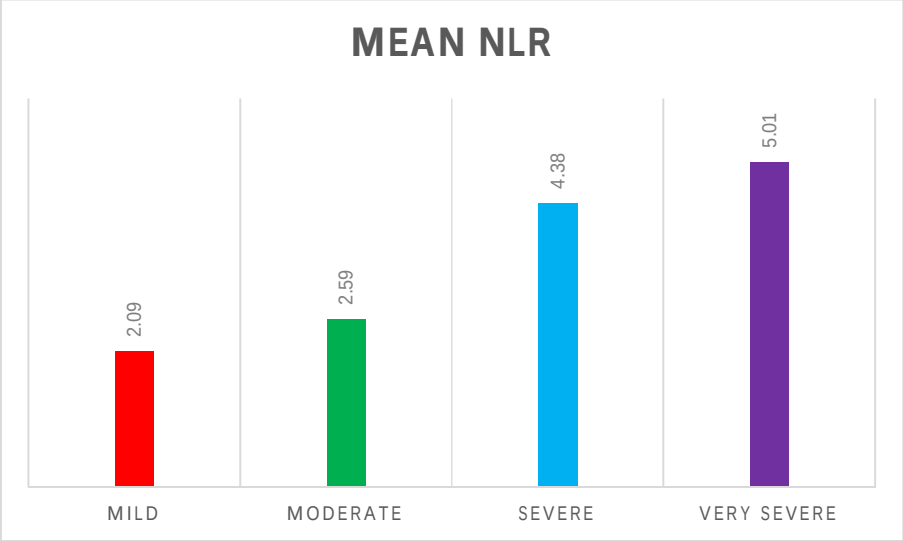


TABLE NO:21- GOLD GRADING OF COPD

GOLD	NO OF PATIENTS	PERCENTAGE
MILD	10	10%
MODERATE	32	32%
SEVERE	17	17%
VERY SEVERE	41	41%

CHART NO:20- GOLD GRADING OF COPD

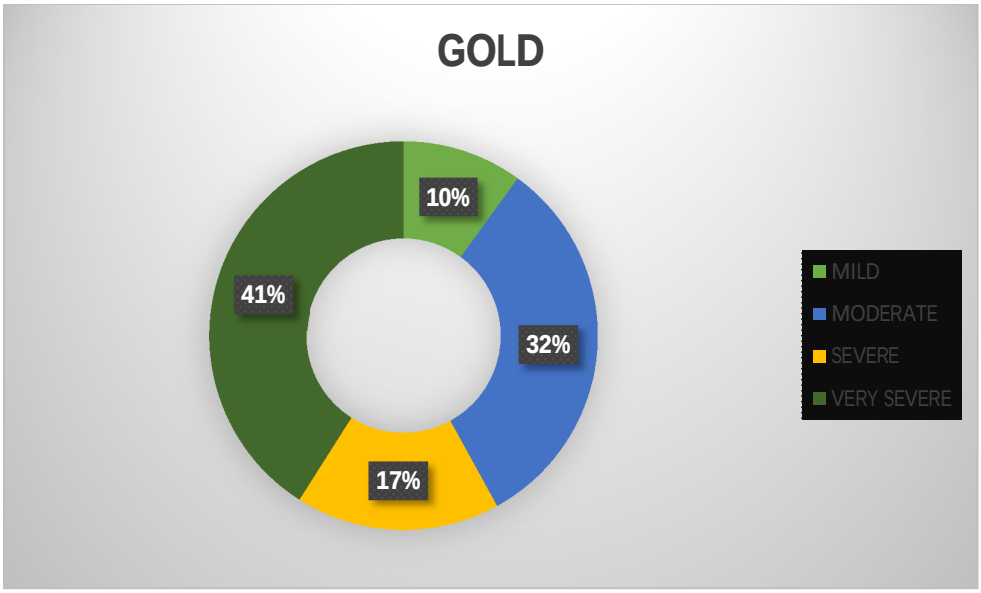


TABLE NO: 22- GOLD GRADING VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

GOLD	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
MILD	2.03	0.47
MODERATE	2.58	1.05
SEVERE	4.29	1.19
VERY SEVERE	5.08	0.86
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

CHART: 21- GOLD GRADING VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

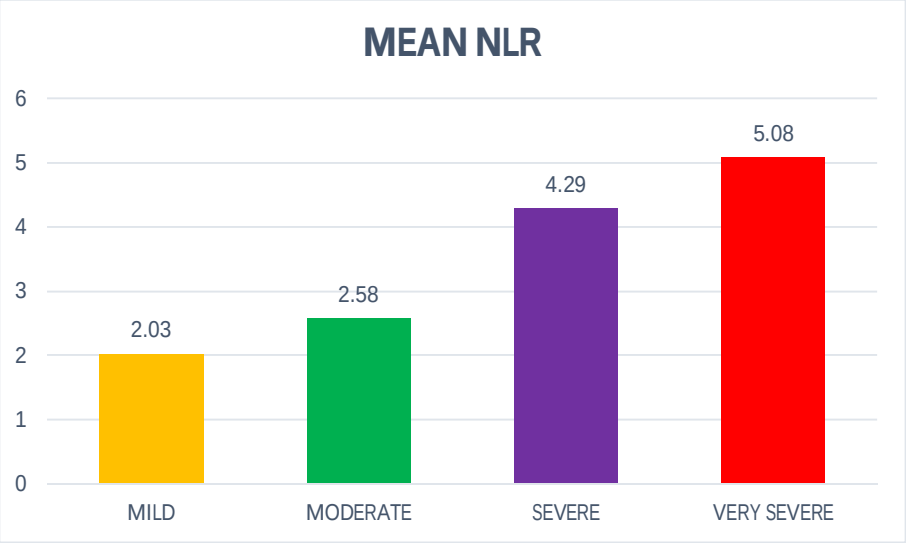


TABLE NO: 23- BODY MASS INDICES OF PATIENTS

BODY MASS INDEX	NO OF PATIENTS	PERCENTAGE
< 18	32	32%
18-23	35	35%
> 23	33	33%

CHART NO: 22- BODY MASS INDICES OF PATIENTS

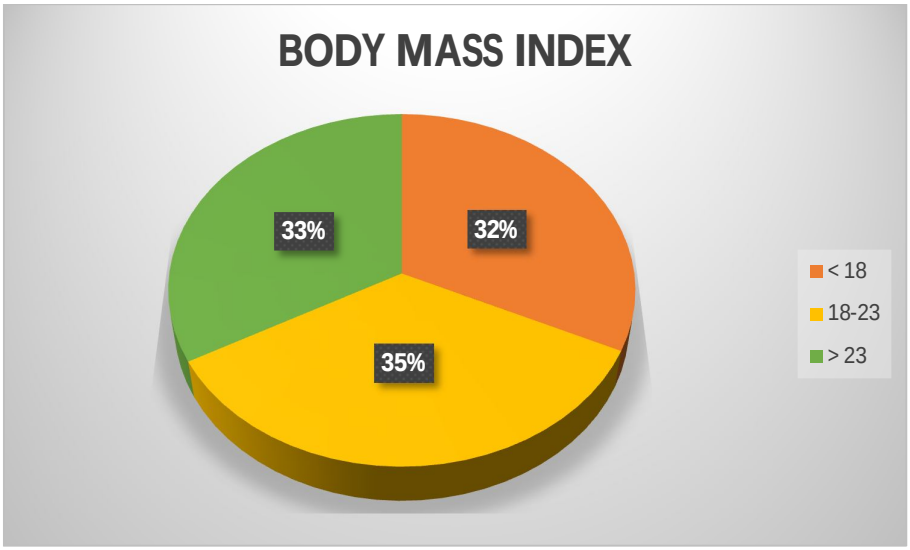


TABLE NO: 24- BODY MASS INDICES VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

BODY MASS INDEX	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
< 50	4.71	1.37
51-60	3.96	1.45
>70	2.97	1.36
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

CHART NO:23- BODY MASS INDICES VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

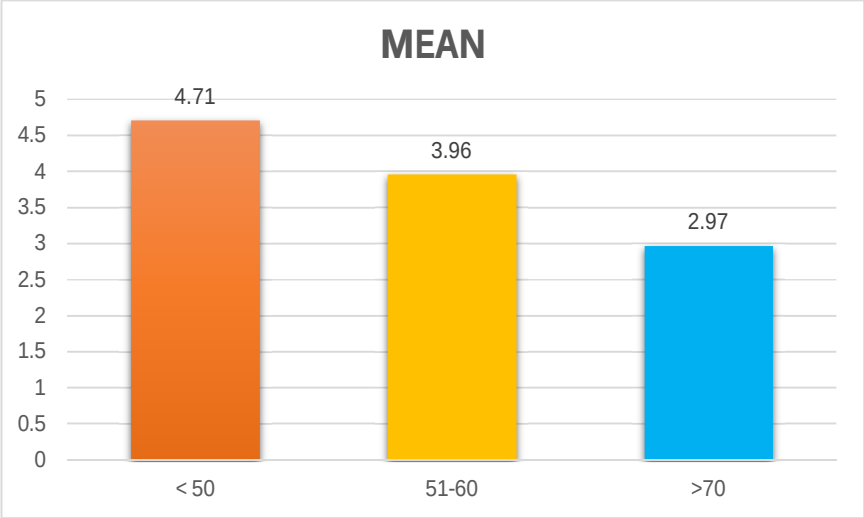


TABLE NO:25- SIX MINUTE WALK DISTANCE

6MWD	NO OF PATIENTS	PERCENTAGE
> 350 MTS	31	31%
250-349 MTS	21	21%
150-249 MTS	17	17%
< 149 MTS	31	31%

CHART NO: 24- SIX MINUTE WALK DISTANCE.

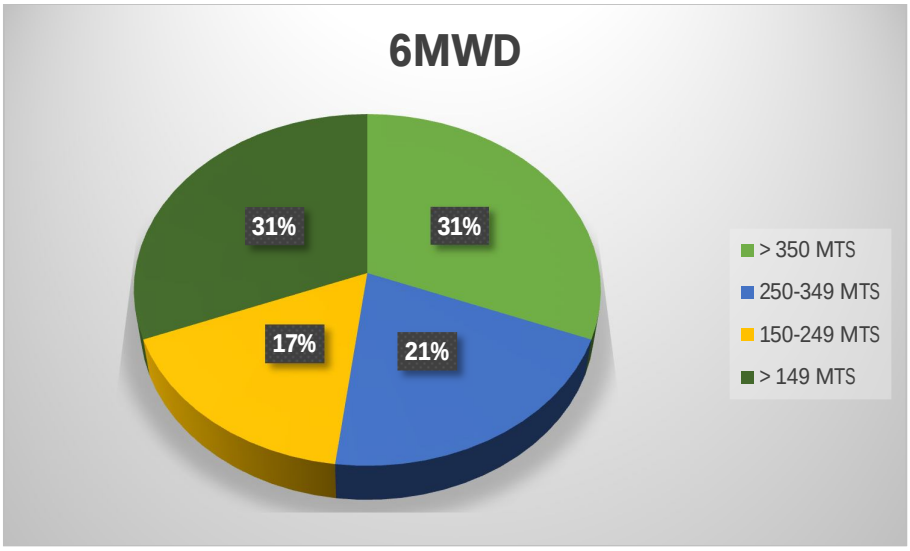


TABLE NO:26- 6 MINUTE WALK DISTANCE VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

6MWD	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
> 350 MTS	2.18	0.81
250-349 MTS	3.87	1.4
150-249 MTS	4.19	1.28
> 149 MTS	5.13	0.89
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

CHART NO:25- 6 MINUTE WALK DISTANCE VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

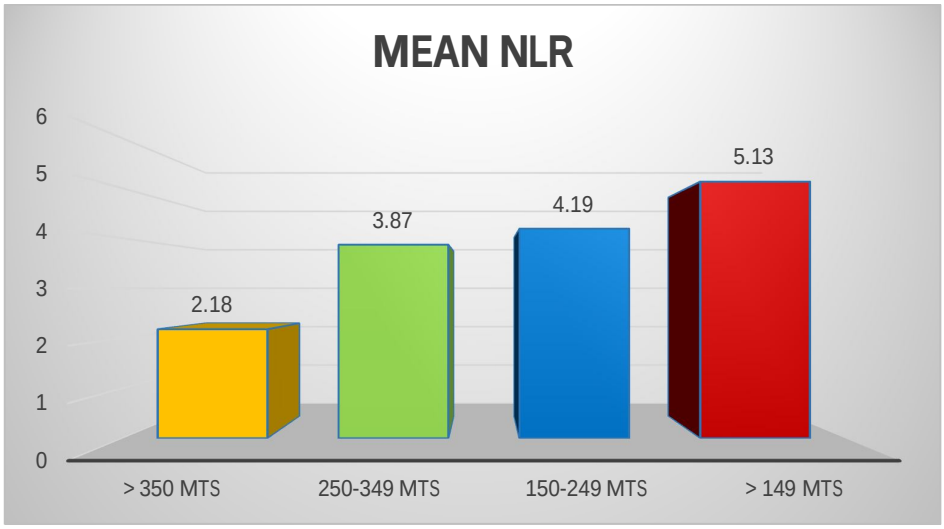


TABLE NO: 27- BODE INDEX OF PATIENTS

BODE INDEX (SURVIVAL %)	NO OF PATIENTS	PERCENTAGE
1(80%)	20	20%
2(67%)	19	19%
3(57%)	20	20%
4(18%)	41	41%

CHART NO:26- BODE INDEX OF PATIENTS

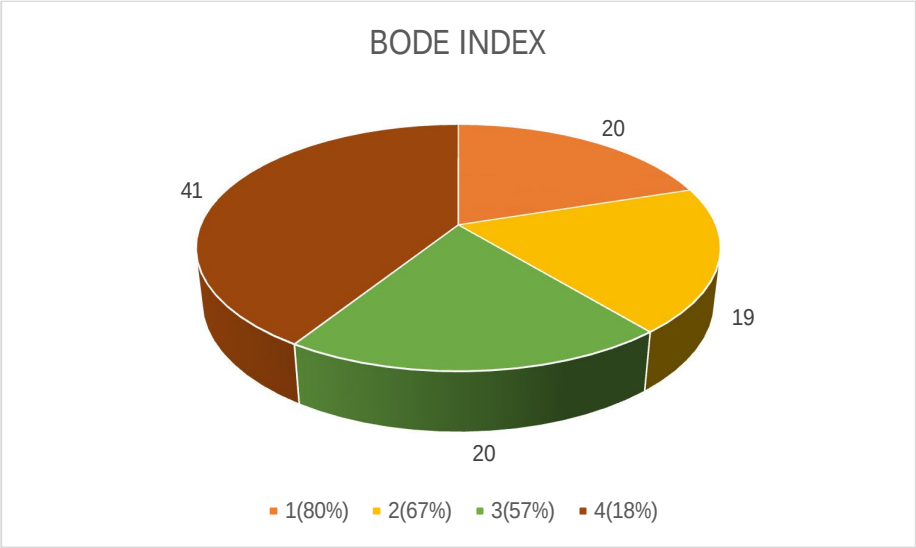


TABLE NO: 28- BODE INDEX VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

BODE INDEX (SURVIVAL %)	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
1(80%)	2.07	0.62
2(67%)	3	1.19
3(57%)	4.25	1.44
4(18%)	4.89	1.04
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

CHART NO:27- BODE INDEX VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

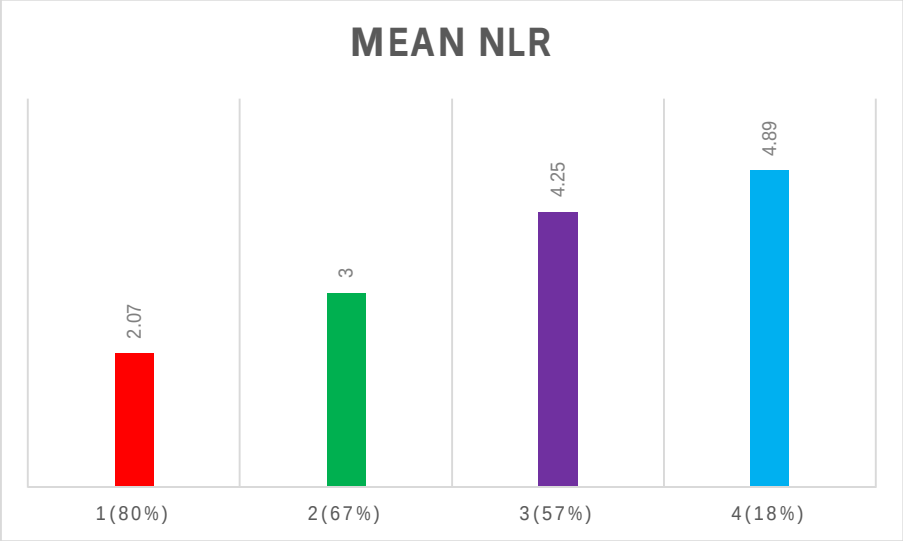


TABLE NO: 29- NUMBER OF PATIENTS WITH PAH

PAH	NO OF PATIENTS	PERCENTAGE
PRESENT	46	46%
ABSENT	54	54%

CHART NO:28- NUMBER OF PATIENTS WITH PAH

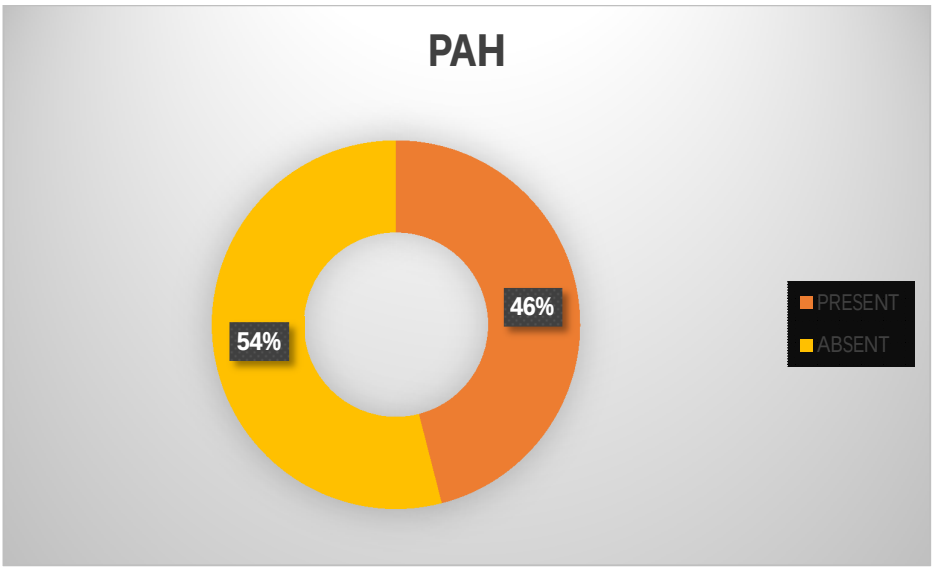


TABLE NO: 30-PAH VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

	NEUTROPHIL LYMPHOCYTE RATIO	
PAH	MEAN	SD
PRESENT	4.81	1.18
ABSENT	3.01	1.35
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO:29-PAH VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

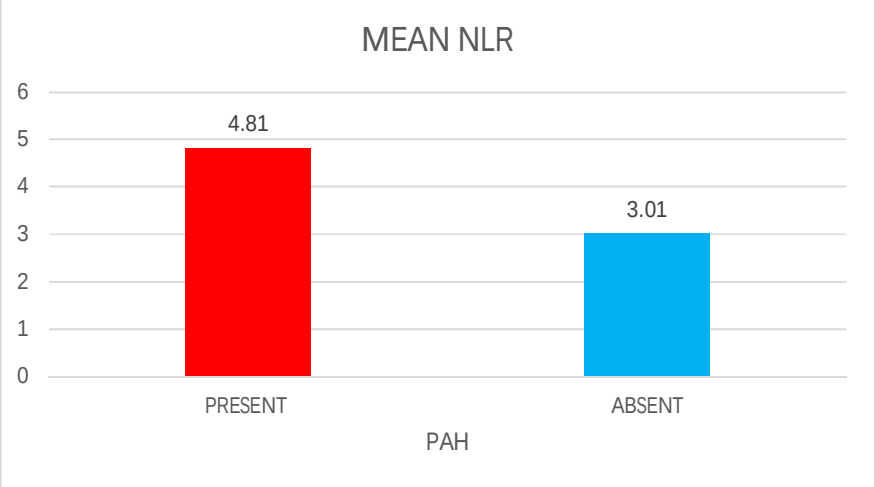


CHART NO:30-PAH VS SEVERITY OF DISEASE

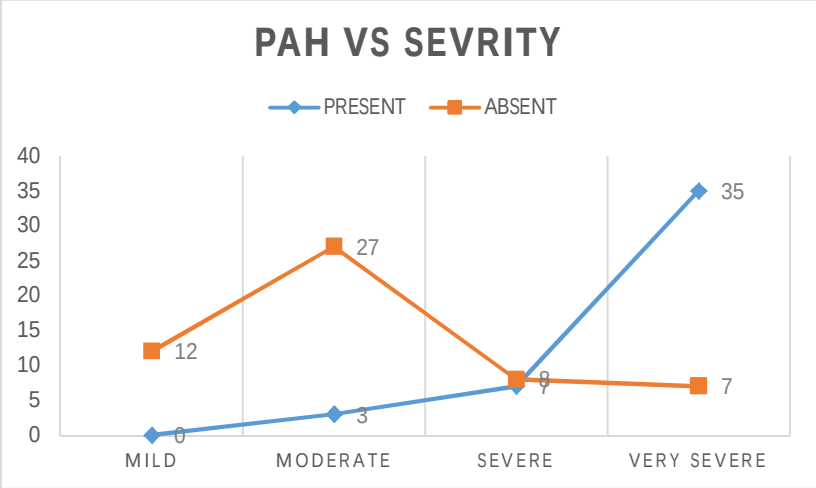


TABLE NO: 31- NUMBER OF PATIENTS WITH FEVER

FEVER	NO OF PATIENTS	PERCENTAGE
PRESENT	34	46%
ABSENT	66	54%

CHART NO:31- NUMBER OF PATIENTS WITH FEVER

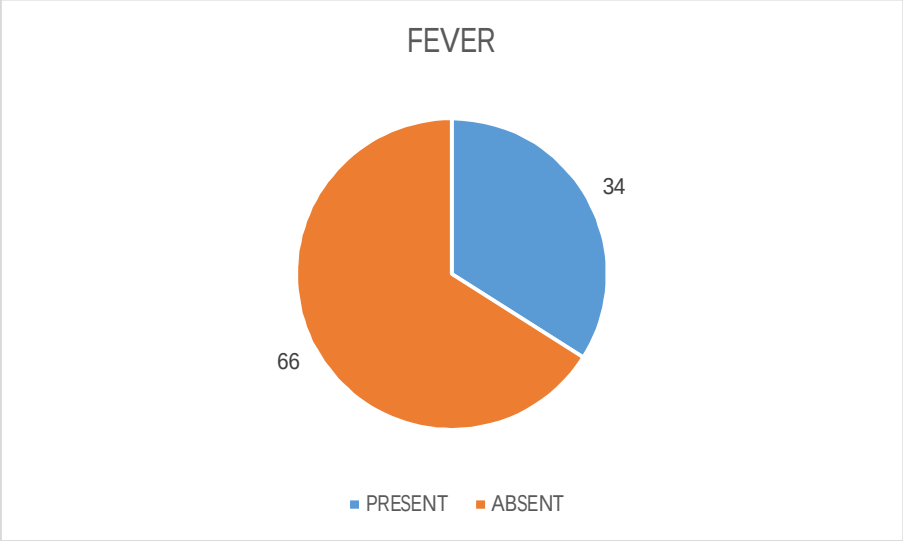


TABLE NO:32- FEVER VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

FEVER	**NEUTROPHIL LYMPHOCYTE RATIO**	
	MEAN	**SD**
PRESENT	4.81	1.19
ABSENT	3.34	1.48
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO:32- FEVER VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

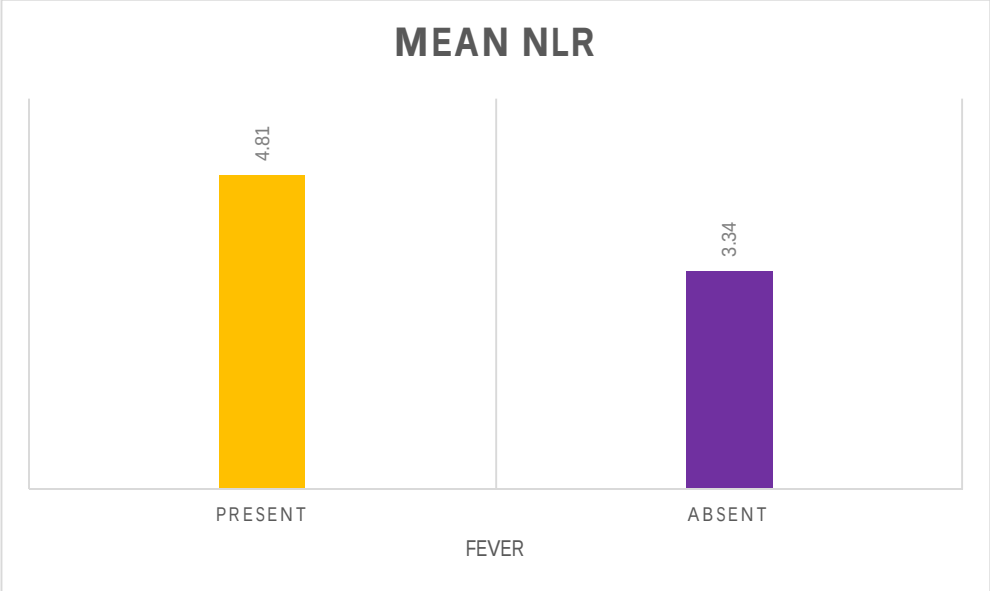


TABLE NO: 33 –FEVER VS FEV1

SEVERITY(FEV1)	FEVER	
	PRESENT	ABSENT
MILD	1	11
MODERATE	1	29
SEVERE	3	12
VERY SEVERE	29	14
P VALUE - 0.001		
SIGNIFICANT		
KRUSKAL WALLIS TEST		

TABLE NO: 34- NUMBER OF PATIENTS HAVING CREPITATIONS

CREPITATION	NO OF PATIENTS	PERCENTAGE
PRESENT	58	58%
ABSENT	42	42%

CHART NO: 33- NUMBER OF PATIENTS HAVING CREPITATIONS

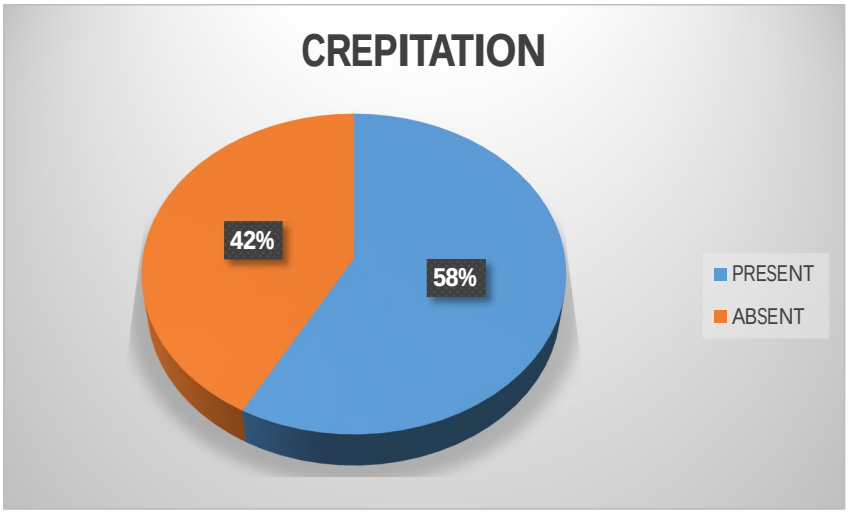


TABLE NO: 35- CREPITATIONS VS MEAN NEUTROPHIL LYMPHOCYE RATIO

CREPITATIONS	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
PRESENT	4.75	1.15
ABSENT	2.58	1.09
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO: 34- CREPITATIONS VS MEAN NEUTROPHIL LYMPHOCYE RATIO

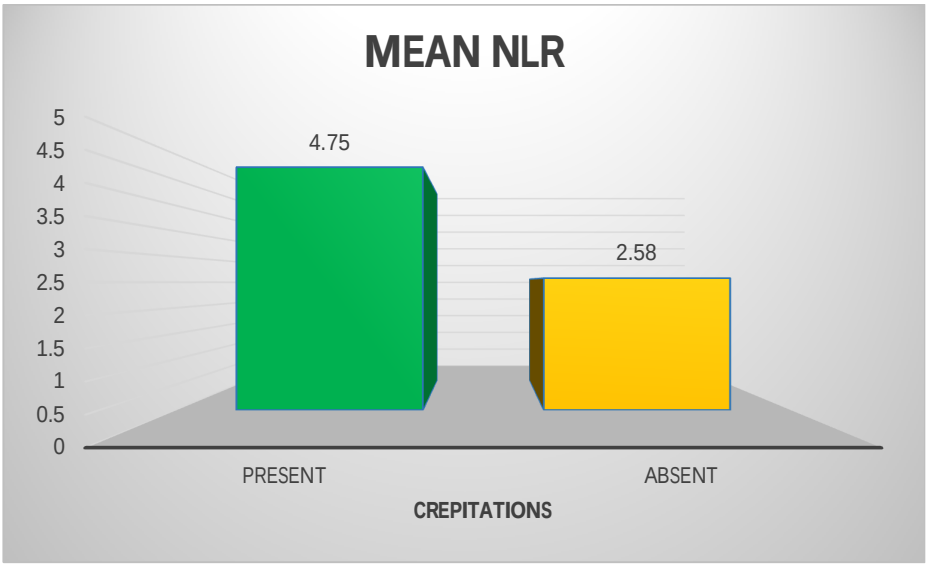


TABLE NO: 36- NUMBER OF PATIENTS HAVING WHEEZING

WHEEZE	NO OF PATIENTS	PERCENTAGE
PRESENT	88	88%
ABSENT	12	12%

CHART NO: 35- NUMBER OF PATIENTS HAVING WHEEZING

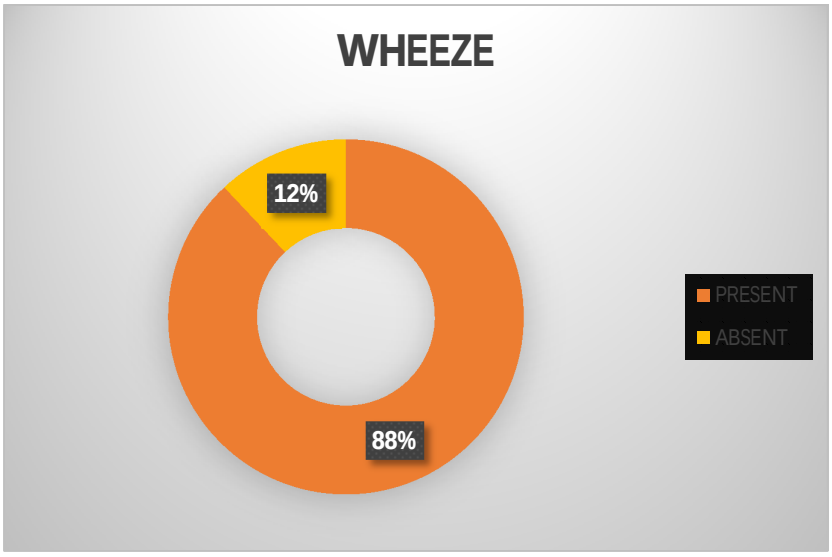


TABLE NO: 37- WHEEZING VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

WHEEZE	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
PRESENT	4.04	1.54
ABSENT	2.34	0.34
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO: 36- WHEEZING VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

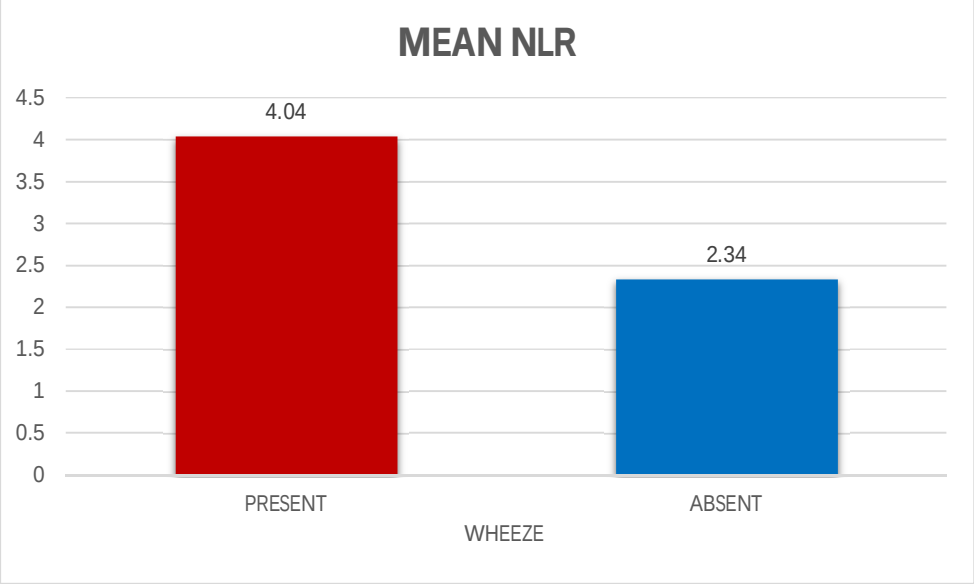


TABLE NO: 38- NUMBER OF PATIENTS HAVING CYANOSIS

CYANOSIS	NO OF PATIENTS	PERCENTAGE
PRESENT	45	45%
ABSENT	55	55%

CHART NO: 37- NUMBER OF PATIENTS HAVING CYANOSIS

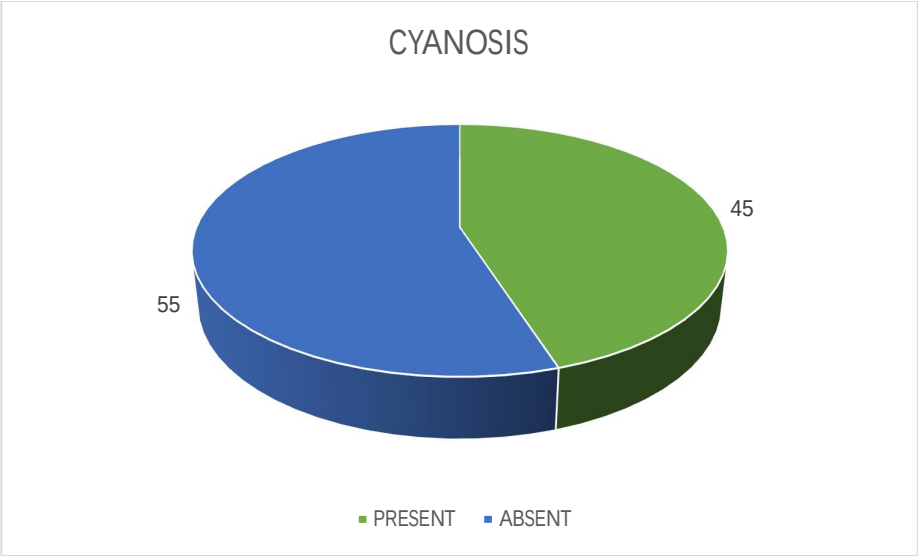


TABLE NO: 39- CYANOSIS VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

CYANOSIS	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
PRESENT	5.07	0.84
ABSENT	2.83	1.25
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO: 38- CYANOSIS VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

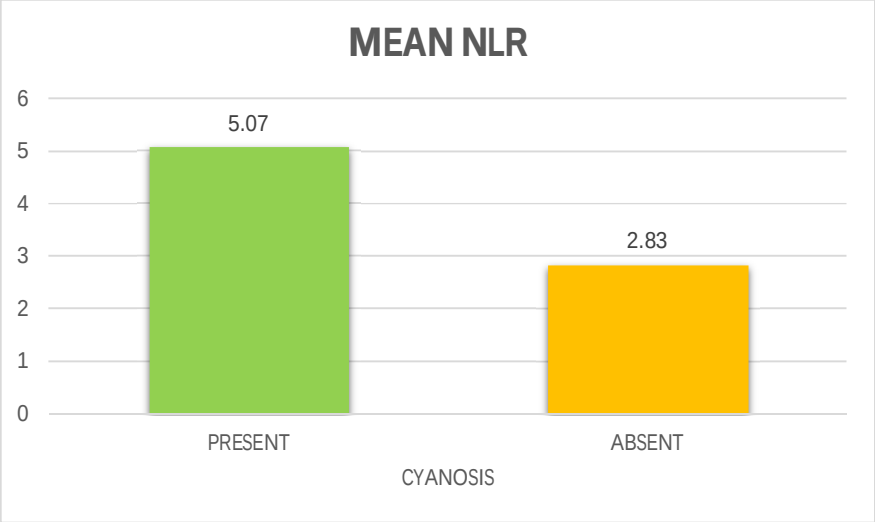


TABLE NO: 40- NUMBER OF PATIENTS HAVING CLUBBING

CLUBBING	NO OF PATIENTS	PERCENTAGE
PRESENT	24	24%
ABSENT	76	76%

CHART NO: 39- NUMBER OF PATIENTS HAVING CLUBBING

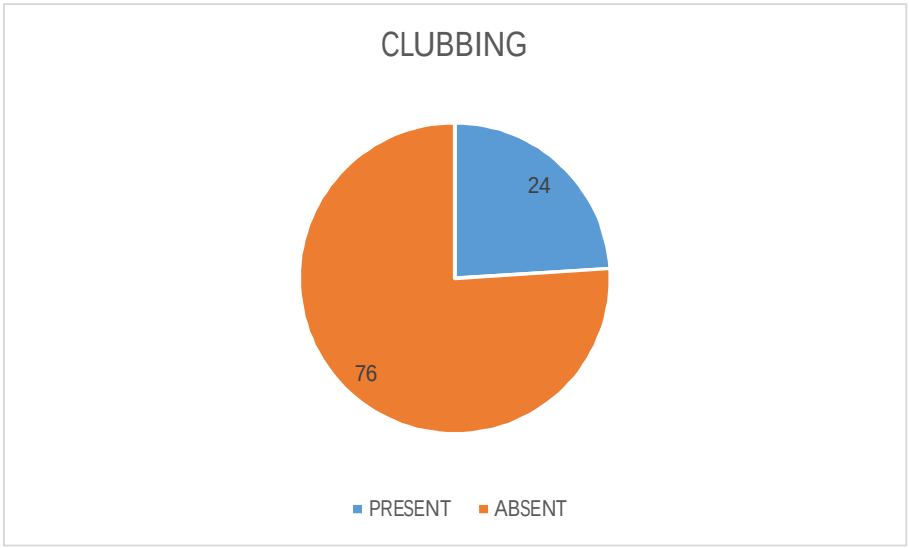


TABLE NO: 41- CULBBING VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

CLUBBING	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
PRESENT	5.13	0.89
ABSENT	3.43	1.49
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO: 40- CULBBING VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

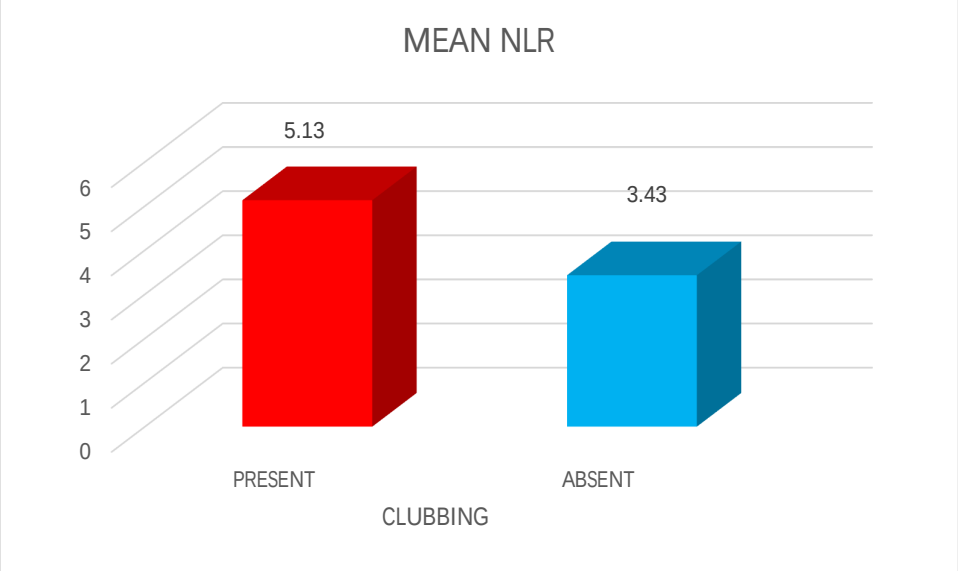


TABLE NO: 42- NUMBER OF PATIENTS WITH PEDAL EDEMA

PEDAL EDEMA	NO OF PATIENTS	PERCENTAGE
PRESENT	43	43%
ABSENT	57	57%

CHART NO: 41- NUMBER OF PATIENTS WITH PEDAL EDEMA

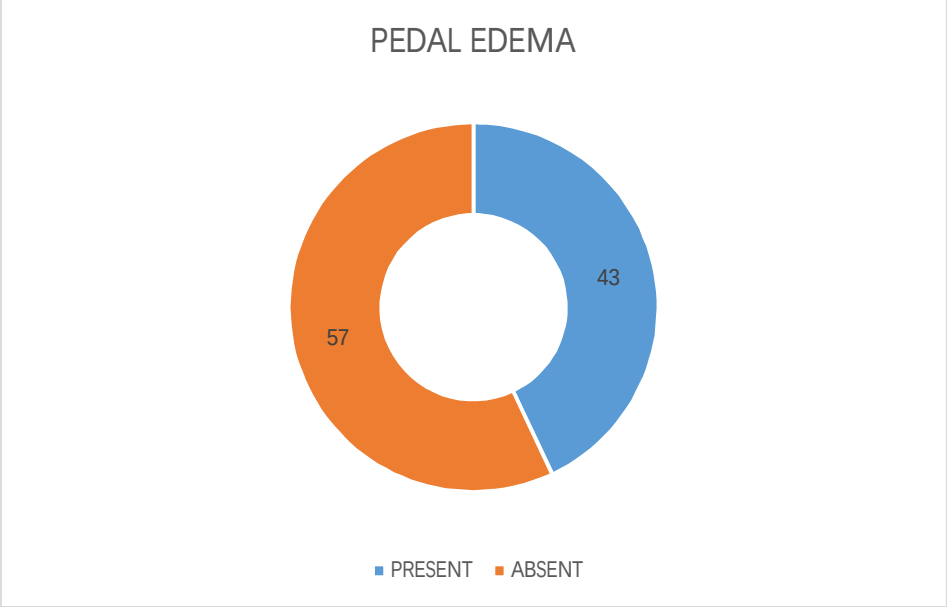


TABLE NO: 43- PEDAL EDEMA VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

PEDAL EDEMA	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
PRESENT	4.78	1.19
ABSENT	3.13	1.41
P VALUE - 0.001		
SIGNIFICANT		
UNPAIRED T TEST		

CHART NO: 42- PEDAL EDEMA VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

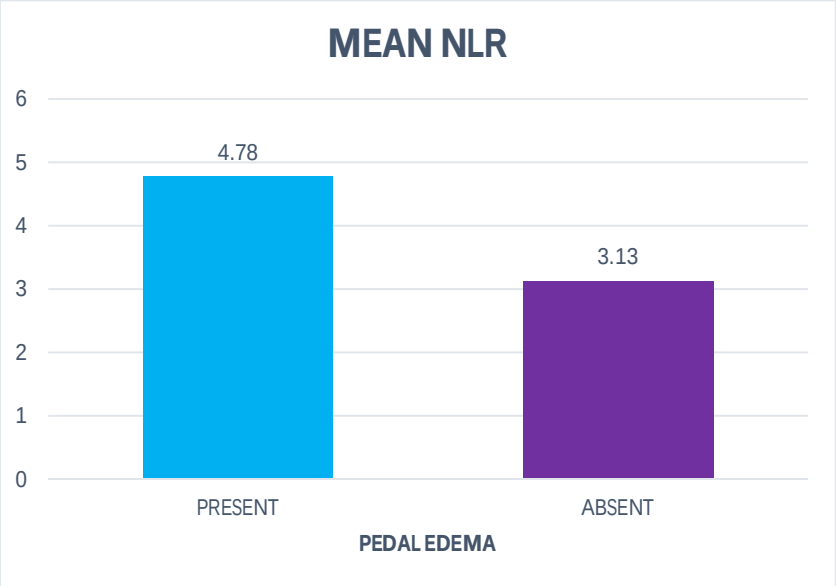


TABLE NO: 44- CHEST X RAY FINDINGS OF PATIENTS

CHEST X RAY	NO OF PATIENTS	PERCENTAGE
EMPHYSEMA & CB	62	62%
EMPHYSEMA	7	7%
CHRONIC BRONCHITIS	28	28%
NORMAL	3	3%

HART NO: 43- CHEST X RAY FINDINGS OF PATIENTS

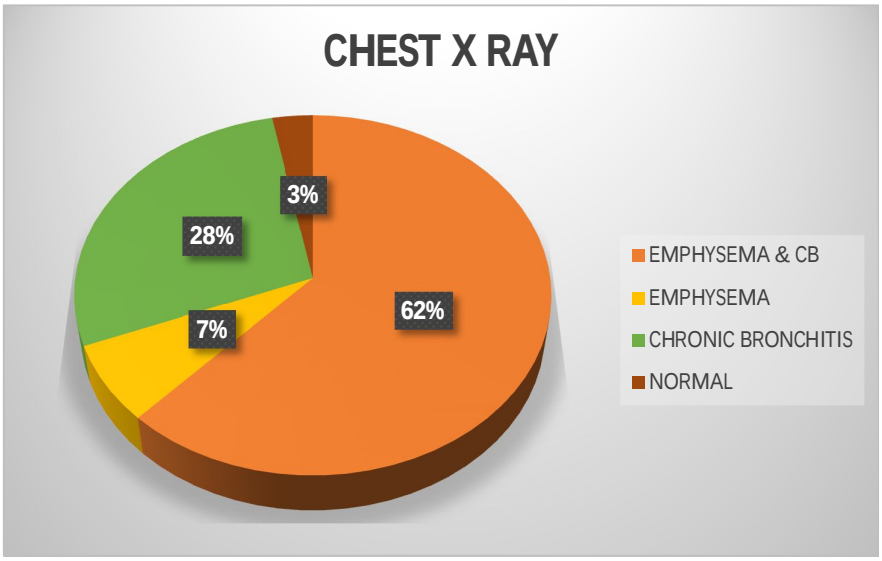


TABLE NO: 45- CHET X RAY VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

CHEST X RAY	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
EMPHYSEMA & CB	4.8	1.07
EMPHYSEMA	2.6	1.22
CHRONIC BRONCHITIS	2.2	0.56
NORMAL	2.04	0
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

CHART NO: 44- CHET X RAY VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

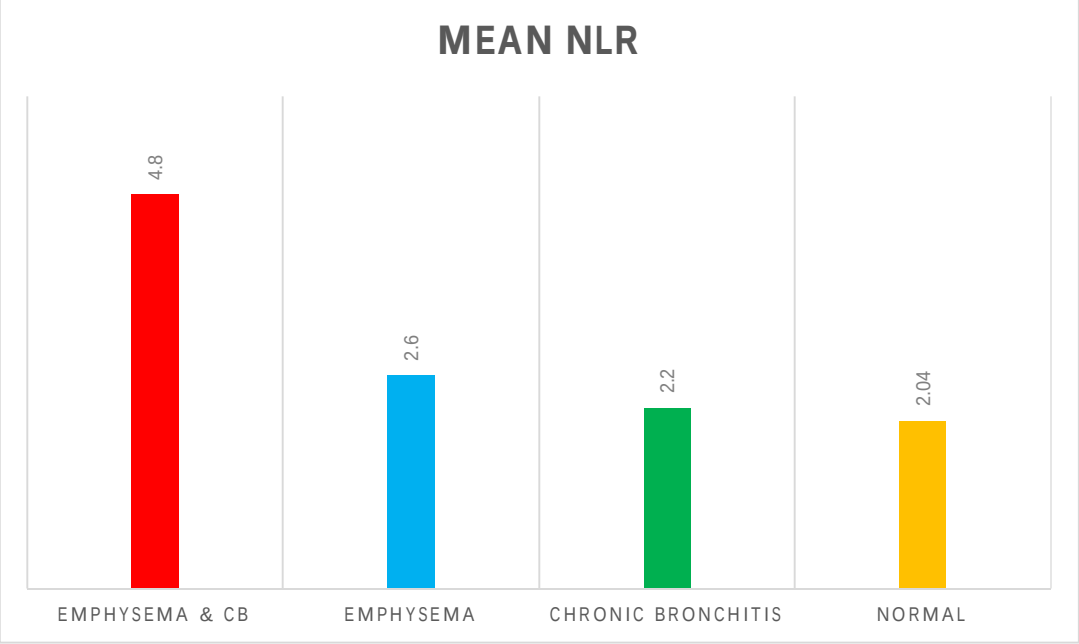


TABLE NO: 46- CT FINDINGS OF PATIENTS

CT CHEST	NO OF PATIENTS	PERCENTAGE
EMPHYSEMA & CB	62	62%
EMPHYSEMA	7	7%
CHRONIC BRONCHITIS	28	28%
NORMAL	3	3%

CHART NO: 45- CT FINDINGS OF PATIENTS

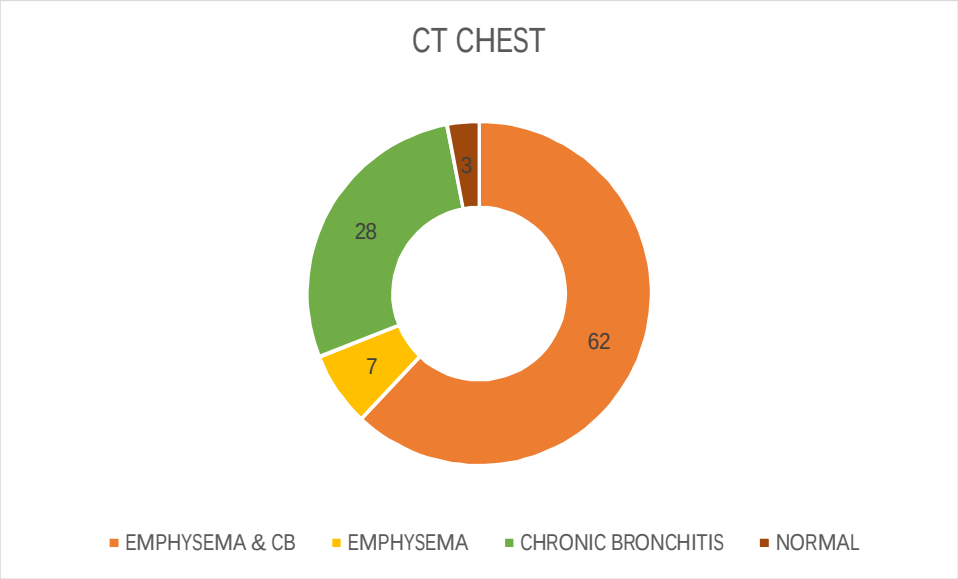


TABLE NO: 47- CT CHEST VS MEAN NEUTROPHIL LYMPHOCYTE RATIO

CT CHEST	NEUTROPHIL LYMPHOCYTE RATIO	
	MEAN	SD
EMPHYSEMA & CB	4.8	1.07
EMPHYSEMA	2.6	1.22
CHRONIC BRONCHITIS	2.2	0.56
NORMAL	2.04	0
P VALUE - 0.001		
SIGNIFICANT		
ANOVA		

DISCUSSION

The study is a cross sectional study pattern where neutrophil lymphocyte ratio was obtained for the COPD patients included in the study, and their disease severity and long term outcome is predicted. The patients who underwent the study were clinically examined along with detailed history was taken and complete blood count and spirometry was done along with the routine investigations.

1. The study included 100 patients, of that 10% had mild, 32% had moderate, 17% had severe and 41% had very severe COPD.

2. Major group (48%) under the study was of age group of 61-70 years, which shows the average age group of the disease in our study.

3. Rural population comprised of 61%, showing major predispondance of COPD to rural areas in our study, and 48% of patients had duration of illness more than 10 years

4. 91% of people participated in study were males, and 9% females, all of the females had biomass fuel exposure so it is considered as the main etiology in them.

5. 68% of patients were smokers, 52% exposed to bio mass fuel and 56% patients had occupational and environmental exposure.

6. All the patients had cough as the major symptom, along with

wheezing and crepitation's were the predominant signs. 46% of patients had fever and absent in 54% and those who had fever had more severe form of exacerbation.

7. 49% of patients had grade 3 severity on MMRC scale followed by 26% Of grade2, 13% of grade 4 and 12% of grade 1 respectively.

8. 43% had very severe restriction based on FEV1, while 30% had moderate, 15% had severe restriction and 12% had mild restriction, showing that almost half the patients had very severe restriction on based of spirometry.

9. Body mass indices of the patients who participated in this study was almost equally divided in all groups of <18, 18-23 and >23 BMI s.

10. The severity of the disease in case of affecting the daily life was shown by 6miniute walk distance in which 31% was not able to walk above 149 meters in 6 minutes, showing the severity of the condition in those patients.

Neutrophil lymphocyte ratio was correlated with each parameters and their results are as follows

1) Age and duration of illness was correlated with NLR, with p value being 0.748 and 0.001 showing its significance towards duration of illness.

2) Those patients who were smokers had high NLR with average of 4.38 compared to the non smoker patients showing that NLR is raised in smoker acute exacerbation COPD patients.

3) The biomass fuel exposure followed the same pattern of smoking as NLR was raised in those patients with exposure compared to normal population with significant with p value (0.005).

4) Place of origin of patient, hypertension were not related in any form with the NLR value.

5) Fever, clubbing, cyanosis, pedal edema, crepitation's, wheezing and PAH showed statistical significance with p value of 0.001, showing that NLR more the severity of the disease is high. Since all the patients had cough p value for the same could not be assessed.

6) The neutrophil lymphocyte ratio was more in patients with more severity of disease shown by MMRC grading, and it indicates that higher the NLR ratio more severe the disease will be on dysponea score.

7) Another important finding is that NLR ratio is inversely related to FEV1 and GOLD grades, with p value being 0.001, which shows the severity of obstruction in airways with more neutrophil lymphocyte ratio.

8) It has been found that NLR was independently correlated with all parameters of BODE index with p value of 0.001.

9) Correlation of chest X ray and CT chest with mean NLR level for emphysema plus chronic bronchitis was 4.8 and showed statistical significance with p value 0.001.

The NLR can be taken as a pulmonary structural and functional indicator, as it is shown that NLR is more in patients with more destruction in lung shown in X ray and CT scan, as the possible mechanism that neutrophils de-granulate causing release of enzymes and result in more emphysematous destruction.

It was also found in this study that NLR was associated with every component of the BODE index and was statistically significant with every component. So it can be said that the walking distance in 6 minutes, the nutritional status of the patient, breathlessness of the patient, every thing severity can be assessed from NLR. Another important thing is that BODE index gives the prognosis and 4year survival rate, so from the simple investigation we can predict somewhat the 4 year prognosis of the patient without costly investigations.

SUMMARY

1) The subjects who participated in the study mostly of age of above 60 years accounting for about 50 % with male to female ratio about 9:1.

2) High ratio of NLR are present is Severe and very severe forms of COPD patients with 41% and 17% patients respectively and their duration of disease was also long.

3) Increased ratio of NLR was found with chronic smoker patients who consisted of 68% of patients.

4) Increased NLR ratio were found in patients with MMRC dyspnea scale of grade 3 and 4 consisting of 49% and 13% respectively.

5) High NLR ratio was found in patients who had both emphysema and chronic bronchitis consisted of 62% of the patients

6) Those who had high BODE index had high level of NLR ratio with 57% four-year survival in 20% patients and 18% four-year survival in 41% patients.

7) Those who had fever had high ratio of NLR who consisted of 46% of the patients included in the study.

8) Those who had crepitation's, wheezing, cyanosis, pedal edema, had high NLR indicating that more severe the disease more the NLR ratio.

9) Subjects with high NLR ratio had low levels of FEV1.

CONCLUSION

Neutrophil lymphocyte ratio is a blood parameter which is easily obtained, and is significantly raised in acute exacerbations of COPD, based on its severity of exacerbation. Those who had more the ratio of NLR indicates more severe the disease. The prognosis and survival rate will be poor in high NLR ratio patients and these patients can be picked up early with the simple investigation-NLR and have to be effectively intervened and rehabilitated to decrease the mortality and morbidity and to have a good quality of life.

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PROFORMA

- Name of the patient:
- Age:
- Sex:
- Duration of disease:
- Place of patient:
- BMI:
- Smoking history:
- Hypertension:
- Biomass Fuel Exposure:
- Environmental exposure:

Symptoms of:

- Cough:
- Fever:
- Wheeze:

Signs of:

- Cyanosis:

- Clubbing:
- PAH:
- Crepitations:
- Pedal edema:
- Findings in chest x ray:
- Findings in CT chest:
- Spirometry reading (pre and post bronchodilator):
- 6MWT –distance walked by patient:
- MMRC grading:
- FEV1:
- GOLD staging:
- BODE index:
- NLR value:

`

ANNEXURE -2

CONSENT FORM

Yourself Mr./Mrs./Ms…….. are being asked to be a participant in the research study titled "**Neutrophil to lymphocyte ratio as a marker of acute exacerbation and disease severity in chronic obstructive pulmonary disease"** in CMC Hospital, Coimbatore, conducted by DR.ANOOP PAULOSE M.D., Post Graduate Student, Department of General Medicine, Coimbatore Medical College. You are eligible after looking into the inclusion criteria. You can ask any question you may have before agreeing to participate.

Research Being Done

Neutrophil to lymphocyte ratio as a marker of acute exacerbation and disease severity in chronic obstructive pulmonary disease

Purpose of Research

To identify the possible correlation between neutrophil to lymphocyte ratio and severity of COPD.

To identify correlation between NLR with pulmonary function test(FEV1) in COPD patients.

To study the prospects of NLR considered to be newer cheaper indicator in acute episodes of COPD

Decline from Participation

You have the option to decline from participation in the study existing protocol for your condition.

Privacy and Confidentiality

Privacy of individuals will be respected and any information about you or provided by you during the study will be kept strictly confidential.

Authorization to publish Results

Results of the study may be published for scientific purposes and/or presented to scientific groups, however you will not be identified.

Statement of Consent

I volunteer and consent to participate in this study. I have read the consent or it has been read to me. The study has been fully explained to me, and I may ask questions at any time.

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Signature /Left thumb impression (volunteer)	Date
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Signature of witness	Date

ஒப்புதல் படிவம்

பெயர் :

வயது :

பாலினம் :

முகவரி:

கோவை அரசு மருத்துவக்கல்லூரி மருத்துவமனையில் மருத்துவர். **mD}g;ghnyh ! ;**தலைமையில் நடைபெறும் இந்த ஆய்வில் முழு சம்மதத்துடன் கலந்துகொள்ள சம்மதிக்கிறேன். இந்த ஆய்வில் என்னை பற்றி விவரங்களை பாதுகாப்புடன் இந்த ஆய்வில் வெளியிட ஆட்சேபணை இல்லை என்று தெரிவித்துக் கொள்கிறேன் .எந்த நேரத்திலும் ஆய்வில் இருந்து எந்த நேரத்திலும் விலக்கிக்கொள்ளும் உரிமை உண்டு என்று அறிவேன் .

இடம் :

தேதி:

கைகெயாப்பம் /ரேகை

KEYS TO MASTER CHART

S.NO – SERIAL NUMBER

BMI – BODY MASS INDEX

MMRC – MODIFIED MEDICAL RESEARCH COUNCIL

BMF – BIO MASS FUEL EXPOSURE

6WMT – 6 MIUTE WALK DISTANCE

GOLD – GLOBAL INITIATIVE FOR COPD

BODE – BODY MASS INDEX, AIRFLOW OBSTRUCTION, DYSPNEA AND EXERCISE

PAH – PULMONARY ARTEY HYPERTENSION

NLR – NEUTROPHIL LYMPHOCYE RATIO

DURATION

1= <5 YEARS

2= 5-10 YRS

3= >10YRS

SMOKING

1= NO

2= YES

ENVIRONMENTAL EXPOSURE

1= NO.

2= YES

HYPERTENTION

1= NO

2= YES

PLACE

1= RURAL

2= URBAN

MMRC (**(Modified Medical Research Council)**

1= GRADE 1

2= GRADE 2

3= GRADE 3

4= GRADE 4

FEV1

1=MILD

2=MODERATE

3=SEVERE

4=VERY SEVERE

GOLD

1= MILD

2=MODERATE

3=SEVERE

4=VERY SEVERE

BMI

1= <18

2= 18-23

3= >23.9

6MWD (6 MINIUTE WALK DISTANCE)

1= >350 METERS.

2= 250-349 METERS

3= 150-249 METERS

4= <149 METERS

BODE INDEX (approximate 4 yr survival)

1=80%

2=67%

3=57%

4=18%

PAH (pulmonary artery hypertension)

1=NO

2=YES

FEVER

1=NO

2=YES

CREPITATIONS

1=NO

2=YES

WHEEZING

1=NO

2=YES

CYANOSIS

1=NO

2=YES

CLUBBING

1=NO

2=YES

PEDAL ODEMA

1=NO

2=YES

CHEST X RAY& CT CHEST

1=EMPHYSEMA & CHRONIC BRONCHITIS

2= EMPHYSEMA

3= CHRONIC BRONCHITIS

4=NORMAL

NEUTROPHIL LYMPHOCYTE RATIO (NLR)

MASTER CHART

S.No	NAME	AGE	SEX	DURATION	SMOKING	ENVIRONMENTAL EXPOSURE	BMF	HYPERTENSION	PLACE	MMRC	FEV1	GOLD	BMI	6MWD	BODE	PAH	FEVER	CREPITATIONS	WHEEZING	CYANOSIS	CLUBBING	COUGH	PEDAL EDEMA	CHEST XRAY	CT CHEST	NLR
1	JAGADEESH	48	M	3	2	1	1	1	2	3	4	4	3	3	4	2	1	2	2	2	1	2	2	1	1	4.56
2	RAMESH	56	M	1	1	2	1	1	1	2	2	2	3	1	1	1	1	1	2	1	1	2	1	4	4	2.04
3	RANGARAJ	65	M	2	2	2	2	1	2	3	4	4	1	2	4	2	2	2	2	2	1	2	2	1	1	5.13
4	SELVARAJ	54	M	3	2	2	1	1	1	4	4	4	2	4	3	2	2	1	2	2	1	2	2	1	1	4.87
5	MANIYAPPAN	66	M	3	2	1	1	1	1	3	2	2	2	2	2	1	1	1	2	1	2	2	1	1	1	4.46
6	SELVAM	55	M	1	2	1	1	2	1	2	2	2	3	1	2	1	1	1	1	1	1	2	1	3	3	2.64
7	MANOJ	66	M	2	2	1	1	1	2	1	1	1	3	1	0	1	1	1	1	1	1	2	1	3	3	2.04
8	NARAYAN	64	M	2	2	2	2	1	2	3	4	4	1	2	4	2	2	2	2	2	1	2	2	1	1	5.87
9	VIGNESH	75	M	1	1	2	2	2	1	2	2	2	3	3	4	1	1	1	2	1	1	2	1	1	1	1.89
10	SHIVARAM	62	M	3	2	1	2	2	1	3	4	4	2	4	4	2	2	2	2	2	2	2	2	1	1	6.01
11	PUSHPA	68	F	1	1	2	2	1	1	2	1	2	2	1	2	1	1	1	2	1	1	2	1	4	4	2.04
12	SHIVSAMMY	71	M	3	2	2	2	2	1	3	4	4	1	4	4	2	2	2	2	2	2	2	2	1	1	5.04
13	AYYASAMI	57	M	1	1	1	1	1	2	1	2	2	3	1	0	1	1	1	2	1	1	2	1	3	3	1.98
14	SIVAKUMAR	67	M	3	2	1	2	2	1	4	4	4	1	4	4	2	2	2	2	2	2	2	2	1	1	4.99

15	SATHEESH	67	M	3	1	1	2	2	1	3	2	2	2	2	3	1	1	1	2	1	1	2	1	3	3	1.99
16	VIYAY	71	M	3	2	2	2	2	1	4	4	4	1	4	4	1	2	2	2	2	2	2	1	1	1	4.45
17	SETHUPATHY	70	M	3	1	1	1	1	2	2	3	3	2	2	3	2	2	2	1	1	1	2	2	2	2	1.98
18	KARTHI	85	M	3	2	2	2	2	1	4	4	4	1	4	4	2	2	2	2	2	2	2	2	1	1	4.44
19	PALRAJ	81	M	3	2	1	1	1	1	3	4	4	3	3	4	2	1	2	2	2	1	2	2	1	1	4.14
20	VISHAK	43	M	1	1	2	1	1	1	2	2	2	3	1	1	1	1	1	2	1	1	2	1	3	3	1.99
21	JOHN	82	M	2	2	2	2	1	2	3	3	3	2	2	2	1	1	2	2	1	1	2	1	1	1	4.06
22	NAGRAJAN	68	M	2	2	2	2	1	1	4	4	4	1	4	4	2	2	2	2	2	2	2	2	1	1	4.94
23	VIRAMUTTHU	49	M	1	2	1	1	1	1	2	2	2	3	2	2	1	1	1	2	1	1	2	1	2	2	4.43
24	PALANI	63	M	1	2	1	2	2	2	2	3	3	3	1	2	1	1	2	1	1	1	2	1	1	1	2.23
25	RAJESH	71	M	3	2	2	1	1	2	3	4	3	2	3	4	2	1	2	2	1	1	2	2	1	1	3.96
26	BANNARII	63	M	2	2	2	2	1	2	3	3	3	2	3	4	1	1	2	1	1	1	2	1	1	1	2.61
27	MUTUCHAMMY	56	M	1	1	1	1	2	2	1	1	1	1	1	1	1	1	1	2	1	1	2	1	3	3	1.77
28	SHIVAKAMI	71	F	3	1	2	2	2	1	3	3	4	3	4	4	2	2	2	2	2	2	2	2	1	1	5.44
29	THAMILSELVI	57	F	2	1	1	2	1	2	2	2	1	2	1	1	1	1	1	2	1	1	2	1	3	3	1.98
30	GOPAL	64	M	3	2	2	2	2	1	3	4	4	1	4	4	2	2	2	2	2	1	2	2	1	1	4.91
31	PANDI	49	M	1	1	1	1	1	2	1	2	2	3	1	1	1	1	1	2	1	1	2	1	3	3	1.79
32	MARAN	67	M	3	2	2	1	2	1	4	4	4	1	4	4	2	1	2	2	2	1	2	1	1	1	4.68
33	MANI	68	M	3	2	2	1	1	1	3	2	2	2	3	3	1	1	1	2	1	1	2	1	3	3	2.04
34	MURUGAN	59	M	3	2	2	1	1	1	3	3	3	1	4	4	1	1	2	2	1	1	2	1	1	1	4.46
35	KITTAN	69	M	3	1	1	2	1	2	3	3	3	2	3	4	2	1	2	2	2	1	2	2	1	1	4.33
36	SAMY	49	M	1	2	2	2	1	1	3	4	4	1	4	3	2	2	2	2	2	2	2	2	1	1	4.76
37	RAJAN	58	M	2	2	1	1	2	1	2	1	1	3	1	1	1	1	1	1	1	1	2	1	3	3	2.03
38	CHANRAMATHI	57	F	2	1	2	2	1	2	3	3	3	1	3	4	1	1	2	2	1	2	2	1	1	1	4.44
39	KANNIAMMAL	66	F	3	1	2	2	2	2	3	4	4	2	3	4	2	2	2	2	2	2	2	2	1	1	5.01

40	RAVEENDRAN	59	M	1	1	2	2	1	1	2	2	2	3	2	2	1	1	1	2	1	1	2	1	2	2	1.93
41	UMASHANKAR	61	M	3	2	1	2	2	1	3	4	4	2	4	4	2	2	2	2	1	1	2	2	1	1	5.07
42	KAMAL	64	M	3	2	2	2	1	1	1	2	2	2	1	1	1	1	1	2	1	1	2	1	3	3	3.06
43	KITTUSAMY	67	M	3	2	2	2	2	1	2	2	2	2	2	2	1	1	1	2	1	1	2	2	2	2	1.98
44	KASHI	70	M	3	2	1	1	1	1	3	4	4	1	3	4	2	2	2	2	2	1	2	2	1	1	4.13
45	VASATHAKUMAR	58	M	1	1	2	1	1	1	2	2	2	3	1	2	1	1	1	2	1	1	2	1	3	3	1.99
46	AYYAVU	65	M	2	2	2	2	1	2	3	4	4	2	2	3	1	1	2	2	1	1	2	1	1	1	4.06
47	AMBI	58	M	2	2	2	2	1	1	4	4	4	1	4	4	2	2	2	2	2	2	2	2	1	1	4.08
48	LOKESHVARAN	67	M	1	2	1	1	1	1	2	2	2	3	2	2	1	1	1	2	1	1	2	1	1	1	4.46
49	MALLIYAMMAL	66	F	2	1	1	2	2	1	2	2	2	3	1	2	1	1	2	1	1	1	2	1	3	3	2.24
50	CHINNASAMY	57	M	3	2	2	1	1	2	3	4	3	2	3	4	2	1	2	2	1	1	2	2	1	1	6.43
51	DEVRAJ	44	M	2	2	2	2	1	2	3	3	3	3	2	3	2	1	2	2	2	1	2	1	1	1	5.91
52	VELUSAMMY	76	M	3	2	2	1	2	2	4	4	4	1	4	4	2	1	2	2	2	2	2	2	1	1	6.98
53	KANAKARAJ	67	M	2	2	1	1	2	2	3	3	3	2	3	3	1	1	2	2	1	1	2	1	1	1	5.65
54	KADHER	65	M	1	1	1	1	2	2	1	1	1	1	1	1	1	2	1	2	1	1	2	1	3	3	1.09
55	VELMURUGAN	58	M	3	2	2	2	2	1	3	4	4	3	4	4	2	2	2	2	2	2	2	2	1	1	5.87
56	PANEERSELVAM	56	M	2	1	1	2	1	2	2	1	2	2	1	1	1	1	1	2	1	1	2	1	3	3	3.98
57	MARI	70	M	3	2	2	2	2	1	3	3	4	1	4	3	2	2	2	2	2	1	2	2	1	1	6.99
58	KADEEJA	65	F	1	1	1	2	1	2	1	2	2	3	1	2	1	1	1	2	1	1	2	1	3	3	2.54
59	ARUCHAMI	63	M	3	2	2	1	2	1	4	4	4	1	4	4	2	1	2	2	2	1	2	1	1	1	5.34
60	ARUMUGAM	84	M	3	2	2	2	1	1	3	2	2	2	3	3	2	1	2	2	1	1	2	2	1	1	1.78
61	MANSOOR	61	M	3	2	2	1	1	1	3	4	3	1	4	4	2	2	2	2	2	1	2	2	1	1	4.98
62	ESHWARAN	66	M	3	1	1	1	1	2	3	3	3	2	2	3	2	1	2	2	2	1	2	2	1	1	4.51
63	PANDIYAN	54	M	1	2	2	2	1	1	3	4	4	1	4	4	1	1	2	2	2	2	2	1	1	1	7.67
64	BASHA	69	M	1	2	1	1	2	1	2	2	1	3	1	1	2	1	1	1	1	1	2	1	3	3	2.35

65	CHINNAYYA	65	M	2	2	2	1	1	2	1	1	1	3	1	1	1	1	1	2	1	1	2	1	3	3	1.87
66	PACHAMUTHU	58	M	1	1	1	1	1	2	1	2	2	3	1	1	2	1	1	2	1	1	2	1	3	3	1.56
67	VEERAN	46	M	3	2	2	1	2	1	4	4	3	1	4	3	3	1	2	2	2	1	2	1	1	1	4.88
68	BALAMURUGAN	71	M	3	2	2	1	1	1	3	2	2	2	3	3	1	1	1	2	1	1	2	1	3	3	2.98
69	ILAYARAJA	71	M	3	2	2	1	1	1	3	4	3	1	4	4	1	1	2	2	1	1	2	1	1	1	3.89
70	SHIVAKUMAR	63	M	3	1	1	2	1	2	3	3	3	2	3	3	2	1	2	2	2	1	2	2	1	1	4.09
71	RAMRAJ	57	M	1	2	2	2	1	1	3	4	4	1	4	3	2	2	2	2	2	2	2	2	1	1	4.99
72	BABU	69	M	1	2	1	1	2	1	2	2	1	3	1	2	1	1	1	1	1	1	2	1	3	3	2.99
73	VELUMANI	64	M	2	2	1	1	1	2	1	1	1	3	1	1	1	1	1	1	1	1	2	1	3	3	2.05
74	CHANDRAN	81	M	2	2	2	2	1	2	3	4	4	1	2	4	2	2	2	2	2	1	2	2	1	1	4.67
75	MOSSES	54	M	1	1	2	2	2	1	2	2	2	3	1	2	1	1	1	2	1	1	2	1	1	1	5.66
76	DEVA	58	M	3	2	1	2	2	1	3	4	4	2	4	4	2	2	2	2	2	2	2	2	1	1	6.04
77	RAMANAN	59	M	1	1	2	2	1	1	2	1	2	2	1	1	1	1	1	2	1	1	2	1	3	3	2.04
78	KARUPPUSAM	53	M	3	2	2	2	2	1	3	4	4	1	4	4	2	2	2	2	2	2	2	2	1	1	5.06
79	KATHIRVEL	65	M	3	2	1	1	1	1	3	4	4	3	3	4	2	1	2	2	2	1	2	2	1	1	4.14
80	MUNIYANDI	59	M	1	1	2	1	1	1	2	2	2	3	1	2	1	1	1	2	1	1	2	1	3	3	1.99
81	MAHALINGAM	49	M	2	2	2	2	1	2	3	3	4	2	2	3	1	1	2	2	1	1	2	1	1	1	4.44
82	FERNADAZ	64	M	3	2	1	1	1	2	3	4	4	3	3	3	2	1	2	2	2	1	2	2	1	1	4.09
83	ELANGOAVAN	65	M	1	1	2	1	1	1	2	1	2	3	1	1	1	1	1	2	1	1	2	1	3	3	2.04
84	PONNAMAL	57	F	2	2	1	2	1	2	3	4	4	2	2	4	2	2	2	2	2	1	2	2	1	1	5.67
85	ISHWARAN	65	M	3	2	2	1	1	1	4	4	4	2	4	3	2	2	1	2	2	1	2	2	1	1	4.81
86	MANIKKAYAM	64	M	3	2	1	1	1	1	3	2	2	2	2	3	1	1	1	2	1	2	2	1	2	2	4.47
87	CHOKKALINGAM	69	M	1	2	1	1	2	1	2	2	2	3	1	2	1	1	1	1	1	1	2	1	3	3	2.82
88	PONNUSAMY	70	M	2	2	1	1	1	2	1	1	1	3	1	1	1	1	1	1	1	1	2	1	3	3	2.13
89	NAGALINGAM	58	M	2	2	2	2	1	2	3	4	4	1	2	3	2	2	2	2	2	1	2	2	1	1	5.87

90	BALUSAMY	56	M	1	1	2	2	2	1	2	2	2	3	1	1	1	1	1	2	1	1	2	1	2	2	1.89
91	PARI	64	M	3	2	1	2	2	1	3	4	4	2	4	4	2	2	2	2	2	2	2	2	1	1	6.01
92	BOOPATHY	66	M	1	1	2	2	1	1	2	1	2	2	1	2	1	1	1	2	1	1	2	1	4	4	2.04
93	KUMAR	56	M	3	2	2	2	2	1	3	4	4	1	4	4	1	2	2	2	2	2	2	2	1	1	5.03
94	VINAYAKAN	70	M	1	1	1	1	1	2	1	2	2	3	1	1	1	1	1	2	1	1	2	1	3	3	1.89
95	RAMAN	56	M	3	1	1	1	1	2	2	2	2	1	2	2	1	2	1	2	1	1	2	2	2	2	1.97
96	DURAISAMY	69	M	3	2	2	2	2	1	4	4	4	1	4	4	1	2	2	2	2	2	2	1	1	1	4.01
97	SARAVANAN	68	M	3	2	1	1	1	1	3	4	4	3	4	4	2	1	2	2	2	2	2	2	1	1	4.56
98	NAGAPPAN	50	M	1	1	1	1	1	1	4	4	4	2	4	4	1	2	2	2	2	1	2	1	1	1	3.99
99	JOSEPH	57	M	2	2	2	2	2	2	3	3	3	2	2	2	1	1	2	2	2	2	2	1	1	1	4.56
100	KARUPPATHAL	63	f	2	2	2	2	2	2	3	3	3	2	2	2	1	1	2	2	2	2	2	1	1	1	4.48